

\*\*\*\*\*STN Columbus \*\*\*\*\*  
\*  
FILE 'HOME' ENTERED AT 09:21:39 ON 20 SEP 1999  
=> file caplus  
COST IN U.S. DOLLARS      ENTRY      SINCE FILE      TOTAL  
FULL ESTIMATED COST      0.15      0.15  
FILE 'CAPLUS' ENTERED AT 09:21:46 ON 20 SEP 1999  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER  
AGREEMENT.  
PLEASE SEE 'HELP USAGE/TERMS' FOR DETAILS.  
COPYRIGHT (C) 1999 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.  
FILE COVERS 1967 - 20 Sep 1999 VOL 131 ISS 13  
FILE LAST UPDATED: 20 Sep 1999 (19990920/ED)  
This file contains CAS Registry Numbers for easy and accurate substance identification.  
This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> s review/dt  
L1 1331380 REVIEW/DT  
=> s (cell?X5aXtherap?)/ab,bi  
1883075 CELL?  
139989 (THERAP?)/AB  
179421 (THERAP?)/BI  
L2 7686 (CELL?X5aXtherap?)/AB,BI  
=> s l1 and l2  
L3 1401 L1 AND L2  
=> s (cell?X3aXtherap?)/ab,bi  
1883075 CELL?  
139989 (THERAP?)/AB  
179421 (THERAP?)/BI  
L4 4796 (CELL?X3aXtherap?)/AB,BI

=> s l4 and l1  
L5 918 L4 AND L1  
=> s l5 and administ?/ab,bi  
368173 ADMINIST?/AB  
397022 ADMINIST?/BI  
L6 41 L5 AND ADMINIST?/AB,BI  
=> s l6 and neuro?/ab,bi  
227772 NEURO?/AB  
301028 NEURO?/BI  
L7 1 L6 AND NEURO?/AB,BI  
=> d bib ab  
L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS  
AN 1997:333476 CAPLUS  
DN 126:338287  
TI Theories and new therapeutics to cure Alzheimers disease  
AU Toledano, Adolfo  
CS Inst. Cajal C.S.I.C., Madrid, Spain  
SO An. R. Acad. Farm. (1996), 62(4), 717-765  
CODEN: ARAFAV; ISSN: 0034-0618  
PB Real Academia de Farmacia  
DT Journal; \*\*\*General Review\*\*\*  
LA Spanish  
AB A review with many refs. Recent theories on Alzheimers disease are opening new treatment lines, both pharmacol. as non-pharmacol. The conviction has already been reached that, in this \*\*\*neurodegenerative\*\*\* illness, it is necessary to plan a global treatment, with all sorts of measures for the patient, including the care-givers, and in which doctors and other sanitary professionals, as well as other social and economic agents, must take part. The aims of these treatments must be considered for every step in the clin. development of each patient given them the highest possible degree of self-sufficiency. Between new drugs being introduced we must emphasize "cholinergic drugs" (ranging from muscarinic agonists to acetylcholinesterase inhibitors), "growth factors" (NGF, gangliosides, \*\*\*neurotrophins\*\*\* and glial factors), neurotrophins (similar in their action to the former), and "aging factor neutralizers" (regulators of intraneuronal calcium and neutralizers or scavengers of free radicals). The anticholinesterase tacrin has shown many secondary effects, due to its hepatotoxicity, but it is hoped that soon, new generation, less

toxic drugs will appear. There are some coadjuvant drugs which can be employed, and others useful in the control of psychotic and depressive symptoms. Even though we cannot yet talk of effective and attainable treatments at this moment, but we can hope that new drug \*\*\*administration\*\*\* routes and pharmacol. approaches (brain injections, slow drug diffusion pumps, \*\*\*neuron\*\*\* and glial \*\*\*cell\*\*\* implants, and gene \*\*\*therapy\*\*\* will, in the near future, be able to control the evolution of the illness.

=> s l4 and neuro?/ab,bi  
227772 NEURO?/AB  
301028 NEURO?/BI  
L8 277 L4 AND NEURO?/AB,BI  
=> d 1-10 bib ab  
L8 ANSWER 1 OF 277 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:577006 CAPLUS  
TI Embryonic or stem-like cell lines produced by cross-species nuclear transplantation  
IN Robl, James; Cibelli, Jose; Slice, Steven L.  
PA University of Massachusetts, A Public Institution of Higher Education of the, USA  
SO PCT Int. Appl., 59 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN/CNT 1  
PATENT NO.      KIND DATE      APPLICATION NO.  
DATE  
PI WO 9945100 A1 19990910 WO 1999-US4608  
19990302  
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 PRAI US 1998:32945 19980302  
 AB An improved method of nuclear transfer involving the transplantation of differentiated donor cell nuclei into enucleated oocytes of a species different from the donor cell is provided. The resultant nuclear transfer units are useful for the prodn. of isogenic embryonic stem cells, in particular human isogenic embryonic or stem cells. These stem-like cells are useful for producing desired differentiated cells and for introduction, removal or modification, of desired genes, e.g., at specific sites of the genome of such cells by homologous recombination. These cells, which may contain a heterologous gene, are esp. useful in \*\*\*cell\*\*\* transplantation \*\*\*therapies\*\*\* and for in vitro study of cell differentiation. Also, methods for improving nuclear transfer efficiency by genetically altering donor cells to inhibit apoptosis, select for a specific cell cycle and/or enhance embryonic growth and development are provided.

L8 ANSWER 2 OF 277 CAPLUS COPYRIGHT 1999 ACS  
 AN 1999:569434 CAPLUS  
 TI Antioxidant activity and biologic properties of a procyanidin-rich extract from pine (pinus maritima) bark, pycnogenol  
 AU Packer, L., Rimbach, G.; Virgili, F.  
 CS Department of Molecular and Cell Biology, University of California, Berkeley, CA, USA  
 SO Free Radical Biol. Med. (1999), 27(5/6), 704-724  
 CODEN: FRBMEH; ISSN: 0891-5849  
 DT Journal  
 PB Elsevier Science Inc.  
 LA English  
 AB There is growing interest in the biol. activities of plant exts. such as that obtained from the bark of the French maritime pine Pinus maritima, Pycnogenol. Pycnogenol (PYC) is a standardized ext. composed of a mixt. of flavonoids, mainly procyanidins and phenolic acids. Studies indicate that PYC components are highly bioavailable. Uniquely PYC displays greater biol. effects as a mixt. than its purified components do individually indicating that the components interact synergistically. PYC has been reported to have cardiovascular benefits, such as a vasorelaxant activity, angiotensin-converting enzyme (ACE) inhibiting activity,

and the ability to enhance the microcirculation by increasing capillary permeability. Investigations of the \*\*\*cellular\*\*\* mechanisms of these \*\*\*therapeutic\*\*\* effects have demonstrated that PYC has strong free radical-scavenging activity against reactive oxygen and nitrogen species. The oligomeric components of PYC contribute significantly to the ESR free radical signal. PYC also participates in the cellular antioxidant network as indicated by its ability to regenerate the radical and to protect endogenous vitamin E and glutathione from oxidative stress. PYC modulates NO metab. in activated macrophages by quenching the NO radical and inhibiting both iNOS mRNA expression and iNOS activity. The spectrum of different effects of NO in the circulation and the nervous system suggest the potential applications of PYC in immune and circulatory disorders as well as in \*\*\*neurodegenerative\*\*\* disease. PYC can bind to proteins, altering their structure and thereby modulating the activity of key enzymes and proteins involved in metabolic pathways. PYC effects redox-sensitive signal transduction pathways and alters gene expression. Aspects of PYC's activity are presented and discussed together with possible future implications and directions in the field of flavonoid research.

L8 ANSWER 3 OF 277 CAPLUS COPYRIGHT 1999 ACS  
 AN 1999:566152 CAPLUS  
 DN 131:167378  
 TI Derivation of cells and tissues from embryonic pre-stem \*\*\*cells\*\*\* for transplantation \*\*\*therapies\*\*\*  
 IN Hodgen, Gary D  
 PA Medical College of Hampton Roads, USA  
 SO PCT Int. Appl., 13 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN/CNT 1  
 PATENT NO. KIND DATE APPLICATION NO.  
 DATE  
 PI WO 9943785 A1 19990902 WO 1999-US4188  
 19990226  
 W: AU, CA, JP, NO  
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
 PRAI US 1998-PV76273 19980227

AB A novel method of isolating and propagating a line of embryonic stem cells that originates from either morulae (pre-stem) or blastocyst (ICM stem cells) is disclosed for the purpose of transplanting cells, tissues or organs.

L8 ANSWER 4 OF 277 CAPLUS COPYRIGHT 1999 ACS  
 AN 1999:565879 CAPLUS  
 TI Isolated stromal cells for use in the treatment of diseases of the central nervous system  
 IN Prockop, Darwin J.; Stokes, David G.; Azizi, S. Ausim; Phinney, Donald G.  
 PA MCP Hahnemann University, USA  
 SO PCT Int. Appl., 138 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN/CNT 1  
 PATENT NO. KIND DATE APPLICATION NO.  
 DATE  
 PI WO 9943286 A2 19990902 WO 1999-US3897  
 19990224  
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 PRAI US 1998-28395 19980224  
 AB Methods of treating a human patient having a disease, disorder or condition of the central nervous system are disclosed. The methods include obtaining a bone marrow sample from a human donor, isolating stromal cells from the bone marrow sample, and administering the stromal cells to the central nervous system of the human patient, wherein the presence of the isolated stromal cells in the brain effects treatment of the disease, disorder or condition. Stromal cells which are isolated may be cultured in vitro, they may be genetically engineered to produce therapeutic compds., and/or they may be pre-differentiated prior to

administration into the central nervous system.

L8 ANSWER 5 OF 277 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:500334 CAPLUS

TI New prospects for human stem- \*\*\*cell\*\*\* \*\*\*therapy\*\*\*  
in the

nervous system

AU Svendsen, Clive N.; Smith, Austin G.

CS MRC Cambridge Centre for Brain Repair, University of  
Cambridge, CB2 2PY,  
UK

SO Trends Neurosci. (1999), 22(8), 357-364

CODEN: TNSCDR, ISSN: 0166-2236

PB Elsevier Science Ltd.

DT Journal

LA English

AB It would be of enormous benefit if human neural tissue could be  
generated  
in vitro as this would allow screening for \*\*\*neuroactive\*\*\*  
comps.,  
and provide a source of tissue for testing \*\*\*cellular\*\*\* and  
gene  
\*\*\*therapies\*\*\* for CNS disorders. It is now well established  
that

pluripotent embryonic stem cells (ES cells) from the mouse can be  
propagated in culture and differentiated into a range of tissues,  
including \*\*\*neuronal\*\*\* and glial cells. In other studies,  
more-restricted neural stem cells have been isolated from both the  
developing and adult rodent brain. Current reports now describe  
similar  
pluripotent and neural stem cells cultured from human  
embryos. While the  
exact nature of these cells continues to be explored, they can be  
grown  
for extended periods of time while retaining the capacity for  
\*\*\*neuronal\*\*\* and glial differentiation. In some cases, they  
have been  
shown to integrate into the developing or damaged adult brain. This  
article

reviews their biol., with a focus on the possible links between  
and neural stem-cell technologies, and the strategies used to isolate  
and  
expand defined cell populations.  
L8 ANSWER 6 OF 277 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:500330 CAPLUS

TI Marrow-mindedness: a perspective on \*\*\*neuropoiesis\*\*\*

AU Scheffler, Bjorn; Horn, Meyer; Blumcke, Ingmar; Laywell, Eric  
D.; Coomes,  
Debra; Kukekov, Valery G.; Steindler, Dennis A.

CS Dept of Anatomy and Neurobiology, University of Tennessee,  
Memphis, TN,  
38163, USA

SO Trends Neurosci. (1999), 22(8), 348-357

CODEN: TNSCDR, ISSN: 0166-2236

PB Elsevier Science Ltd.

DT Journal

LA English

AB There are pluripotent stem cells in the adult brain that might not  
be very  
different from those found in bone marrow. Recent and profound  
advances

in the field of \*\*\*neuropoiesis\*\*\*, which often rely on insights  
from  
studies of hematopoiesis and in some instances use cross-paradigms  
with  
this field, have already revealed that bone marrow has much in  
common with  
so-called 'brain marrow'. Proliferative primogenitors and  
developmentally  
regulated mols. are hallmarks of both \*\*\*neuropoiesis\*\*\* and  
hematopoiesis. This article will focus on recent advances in  
\*\*\*neuropoiesis\*\*\* within a central core of the mature brain  
that is  
referred to as brain marrow, discussing its pluripotency and  
proliferative

capacity, in vitro and mol. assays used in its study, and markers of  
\*\*\*neuropoietic\*\*\* stem/progenitor cells. As hematopoiesis  
research has  
led to the discovery of numerous morphogenetic factors, it is  
anticipated  
that studies of \*\*\*neuropoiesis\*\*\* should also uncover many  
new  
factors and genes that affect the growth and differentiation of neural  
inclusion of  
rationale for the persistence of normal stem/progenitor cells even in  
the

aged brain. By analogy with hematopoiesis research, a thorough  
investigation of brain marrow should provide basic insights into  
developmental and persistent \*\*\*neurogenesis\*\*\* while  
anticipating  
\*\*\*cell\*\*\*-transplant and gene \*\*\*therapies\*\*\* for  
debilitating  
\*\*\*neuro\*\*\* diseases.  
L8 ANSWER 7 OF 277 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:483394 CAPLUS  
DN 131:111455

TI Methods of treatment using MAO-A and MAO-B inhibitors such  
as L-deprenyl  
PA USA  
IN Thomas, Thomas N.  
SO PCT Int. Appl., 42 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN/CNT 1

PATENT NO. KIND DATE APPLICATION NO.  
DATE

PI WO 93/7293 A2 19990729 WO 1999-US1670  
19990126

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,  
CU, CZ, DE,

DK, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN,  
IS, JP,

KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,  
MG, MK, MN,

MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,  
SL, TI, TM,

TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG,  
KZ, MD, RU,  
TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH,  
CY, DE, DK, ES,

FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BI, CF,  
CG, CI,

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-PV72718 19980127

AB Effects of MAO-A or MAO-B inhibitors such as L-deprenyl on  
both cerebral  
and peripheral vasculature, on nonvascular smooth muscle, on the  
nervous  
system, and on platelets, RBC, WBC, mast cells, macrophages, and  
glial  
cells are disclosed. The effects are the result of a mode of action  
for

MAO-A or MAO-B inhibitors such as L-deprenyl which is totally  
unrelated to  
selective inhibition of MAO-A and/or MAO-B. Therapeutic  
methods of using  
MAO-A or MAO-B inhibitors such as L-deprenyl to treat a variety  
of  
disorders are disclosed.

L8 ANSWER 8 OF 277 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:468044 CAPLUS  
DN 131:125922

TI Method for preventing and treating sensorineural hearing loss and  
vestibular disorders using glial cell line-derived

\*\*\*neurotrophic\*\*\*

factor (GDNF) protein product

IN Magal, Ella

PA Amgen Inc., USA

SO U.S., 24 PP., Cont.-in-part of U. S. 5,837,681.

CODEN: USXXAM

DT Patent

LA English

FAN/CNT 2

PATENT NO. KIND DATE APPLICATION NO.  
DATE

PI US 5929041 A 19990727 US 1996-710219 19960913  
US 5837681 A 19981117 US 1996-606176 19960223

WO 9730722 A1 19970828 WO 1997-US2677

19970214

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,  
CU, CZ, DE,

DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR,

KZ, LC,  
LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,  
NO, NZ, PL, PT,  
RO, RU, SD, SE, SI, SK, TJ, TM, TR, TT, UA, UG, UZ,  
VN, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI,  
FR, GB, GR,  
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,  
GN, ML,  
MR, NE, SN, TD, TG  
CA 1997-2217565 19970214  
AU 9722779 A1 19970910 AU 1997-22779 19970214  
AU 691443 B2 19980514  
EP 822829 A1 19980211 EP 1997-906022 19970214  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
MC, PT,  
IE, SI, LT, LV, FI, RO  
CN 1181704 A 19980513 CN 1997-190100 19970214  
JP 11504351 T2 19990420 JP 1997-530323 19970214  
NO 9704767 A 19971222 NO 1997-4767 19971015  
PRAI US 1996-606176 19960223  
US 1996-710219 19960913  
WO 1997-US2677 19970214  
AB The present invention relates generally to methods for preventing  
and/or  
treating injury or degeneration of cochlear (and vestibular) hair  
cells  
and spiral ganglion \*\*\*neurons\*\*\* by administering glial cell  
line-derived \*\*\*neurotrophic\*\*\* factor (GDNF). The invention  
relates  
more specifically to methods for treating sensorineural hearing loss  
adn  
vestibular disorders. Thus, at 8 days after treatment of 4 guinea  
pigs  
with cisplatin the loss of hair cells in the middle turn of the cochlea  
was 34, 47, 42, and 41%, resp.; whereas, after injection of GDNF  
(1 mg/mL)  
into the right middle ear, the hair cell loss was reduced to 16, 23,  
21,  
and 29%, resp.

L8 ANSWER 9 OF 277 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:464356 CAPLUS  
DN 131:33970  
TI Feline immunodeficiency virus gene therapy vectors  
IN Johnston, Julie C.; Sauter, Sybille L.; Hsu, David; Sheridan,  
Philip Lee;  
Hardy, Stephen F.; Dubensky, Thomas W.; Yee, Jung-Kuan  
PA Chiron Corporation, USA  
SO PCT Int. Appl., 170 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN/CNT 1  
PATENT NO. KIND DATE APPLICATION NO.  
DATE

PI WO 9936511 A2 19990722 WO 1999-US11194  
19990119  
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,  
CU, CZ, DE,  
DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS,  
JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG,  
MK, MN, MW,  
MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,  
TM, TR,  
TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ,  
MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH,  
CY, DE, DK, ES,  
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
CG, CI,  
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
PRAI US 1998-71731 19980116  
US 1998-86825 19980526  
US 1999-114955 19990104  
US 1999-231235 19990115  
AB Disclosed are gene therapy vectors based upon the feline  
immunodeficiency  
virus, as well as related packaging cell lines, methods for prodn.,  
and  
methods of use.

L8 ANSWER 10 OF 277 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:452502 CAPLUS  
TI In Vitro Expansion of a Multipotent Population of Human Neural  
Progenitor  
Cells  
AU Carpenter, Melissa K.; Cui, Xia, Hu, Zhong-yi; Jackson,  
Jennifer; Sherman,  
Sandy; Seiger, ANG ke; Wahlberg, Lars U.  
CS Cell and Molecular Neurobiology, CytoTherapeutics, Inc.,  
Lincoln, RI,  
02865, USA  
SO Exp. Neurol. (1999), 158(2), 265-278  
CODEN: EXNEAC; ISSN: 0014-4886  
PB Academic Press  
DT Journal  
LA English  
AB The isolation and expansion of human neural progenitor cells  
have  
important potential clin. applications, because these cells may be  
used as  
graft material in \*\*\*cell\*\*\* \*\*\*therapies\*\*\* to regenerate  
tissue  
and/or function in patients with central nervous system (CNS)  
disorders.  
This paper describes a continuously dividing multipotent  
population of  
progenitor cells in the human embryonic forebrain that can be  
propagated  
in vitro. These cells can be maintained and expanded using a

serum-free  
defined medium contg. basic fibroblast growth factor (bFGF),  
leukemia  
inhibitory factor (LIF), and epidermal growth factor (EGF). Using  
these  
three factors, the cell cultures expand and remain multipotent for at  
least 1 yr in vitro. This period of expansion results in a 107-fold  
increase of this heterogeneous population of cells. Upon  
differentiation,  
they form \*\*\*neurons\*\*\*, astrocytes, and oligodendrocytes, the  
three  
main phenotypes in the CNS. Moreover, GABA-immunoreactive  
and tyrosine  
hydroxylase-immunoreactive \*\*\*neurons\*\*\* can be identified.  
These  
results demonstrate the feasibility of long-term in vitro expansion  
of  
human neural progenitor cells. The advantages of such a population  
of  
neural precursors for allogeneic transplantation include the ability  
to  
provide an expandable, well-characterized, defined cell source  
which can  
form specific \*\*\*neuronal\*\*\* or glial subtypes. (c) 1999  
Academic  
Press.

=> s 12 and neuro?/ab, bi  
227772 NEURO?/AB  
301028 NEURO?/BI  
L9 485 L2 AND NEURO?/AB, BI  
=> s 19 and 11  
L10 66 L9 AND L1  
=> d 1-10 bib ab

L10 ANSWER 1 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:432617 CAPLUS  
DN 131:114087  
TI Identification of neural stem \*\*\*cells\*\*\* and its application to  
the  
\*\*\*therapeutics\*\*\* of damaged brains  
AU Kawaguchi, Ayano; Okano, Hideyuki  
CS Biomed. Res. Cent. Osaka Univ. Grad. Sch. Med., Japan  
SO Saishin Igaku (1999), 54(7), 1721-1729  
CODEN: SAIGAK; ISSN: 0370-8241  
PB Saishin Igakusha  
DT Journal, \*\*\*General Review\*\*\*  
LA Japanese  
AB A review, with 22 refs., on \*\*\*neuronal\*\*\* development in  
fetal stage  
of mammals, establishment of selective culture of neural stem cell,

study on its differentiation regulation, existence of neural stem cell in adults, and possibility of clin. application of neural stem cells.

L10 ANSWER 2 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:299361 CAPLUS  
DN 131:128230  
TI \*\*\*Neuroendocrine\*\*\* differentiation in prostatic carcinoma  
AU Abrahamsson, Per-Anders  
CS Department of Urology, University Hospitals of Malmo and Lund, University of Lund, Lund, S-221 85, Swed.  
SO Prostate (N. Y.) (1999), 39(2), 135-148  
CODEN: PRSTD; ISSN: 0270-4137  
PB Wiley-Liss, Inc.  
DT Journal; \*\*\*General Review\*\*\*  
LA English  
AB A review, with 159 refs. Information is presented on prostatic \*\*\*neuroendocrine\*\*\* cells and \*\*\*neuroendocrine\*\*\* differentiation in prostatic carcinoma. The prognostic and therapeutic implications of \*\*\*neuroendocrine\*\*\* differentiation in prostatic carcinoma are reviewed. Data are presented that support the intriguing link between \*\*\*neuroendocrine\*\*\* differentiation, tumor progression, and androgen-independent prostate cancer. The hormones, and the receptors, expressed by prostatic \*\*\*neuroendocrine\*\*\* cells are investigated in order to elucidate their significance for prognosis and therapy. The prognostic significance of \*\*\*neuroendocrine\*\*\* differentiation in prostatic malignancy has been controversial, but recent studies employing markers such as chromograin A and \*\*\*neuron\*\*\*-specific enolase suggest that \*\*\*neuroendocrine\*\*\* differentiation, as reflected by increased tissue expression and/or blood levels of these \*\*\*neuroendocrine\*\*\* secretory products, correlates with poor prognosis, tumor progression, and androgen-independence. Since all malignant \*\*\*neuroendocrine\*\*\* cells are devoid of androgen receptors and since \*\*\*neuroendocrine\*\*\* phenotypic expression is not suppressed by androgen ablation, clonal propagation of androgen receptor-neg. \*\*\*neuroendocrine\*\*\* cells may play an important role in the pathway towards the androgen-independent state of prostatic carcinoma. This would have significant implications for the treatment of prostate cancer, as several of the hormones known to be expressed by \*\*\*neuroendocrine\*\*\* -differentiated, malignant prostatic \*\*\*cells\*\*\* are potential

candidates for drug \*\*\*therapy\*\*\*. A limited no. of hormones have been tested in this context, in particular somatostatin, bombesin, and serotonin. \*\*\*Neuroendocrine\*\*\* differentiation in carcinoma of the prostate appears to be assoc. with poor prognosis, tumor progression, and the androgen-independent state, for which there is currently no successful therapy. Therefore, new therapeutic protocols and trials need to be developed to test drugs based on \*\*\*neuroendocrine\*\*\* hormones and/or their antagonists. An evaluation of this new therapeutic approach against prostatic carcinoma with \*\*\*neuroendocrine\*\*\* differentiation, including hormone-refractory cancer, is easily justified, since these tumors are unresponsive to current modes of therapy.

L10 ANSWER 3 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:237724 CAPLUS  
DN 131:39041  
TI The therapeutic potential of CXCL chemokine blockade in acute inflammation in the brain  
AU Anthony, Daniel C.; Walker, Katherine; Perry, V. Hugh  
CS CNS Inflammation Group, Centre for Neuroscience at Southampton, University of Southampton, SO16 7PX, UK  
SO Expert Opin. Invest. Drugs (1999), 8(4), 363-371  
CODEN: EOIDR; ISSN: 1354-3784  
PB Ashley Publications  
DT Journal; \*\*\*General Review\*\*\*  
LA English  
AB A review with 63 refs. Mammalian \*\*\*neurons\*\*\* of the central nervous system (CNS) are terminally differentiated, and there is little endogenous capacity of the CNS to repair itself. Peripheral tissue injury, disease or infection results in a stereotypical inflammatory response to protect the host from pathogens and to promote tissue repair. However, collateral or "bystander" damage is characteristic of any inflammatory response. Thus, it is apparent that the CNS has evolved mechanisms to regulate tightly the acute inflammatory response, and in particular to restrict the recruitment of neutrophils, in an attempt to protect itself from the potentially damaging consequences of inflammation in the brain. However, neutrophils are not always excluded from the brain. Indeed, they are found in large nos. in the brain parenchyma following traumatic lesions,

stroke lesions, and in rodents, during the "window of susceptibility". \*\*\*Therapy\*\*\* targeted at blocking excitotoxic death has not successfully transferred from rodent models of stroke to human stroke patients. Restricting leukocyte entry to the brain, thereby inhibiting the inflammatory response, may prove to be a more practical therapeutic approach. The evidence presented in this review suggests that antagonizing the effects of CXCL chemokines may represent one route to achieve this goal.

L10 ANSWER 4 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:169142 CAPLUS  
DN 131:3046  
TI Apoptosis: molecular mechanisms  
AU Solary, Eric  
CS Unite INSERM 517, Mort cellulaire et cancer, Groupe Biologie et Therapie des Cancers (JES15), Facultes de Medecine et de Pharmacie, Dijon, 21033, Fr.  
SO C. R. Seances Soc. Biol. Ses Fil. (1998), 192(6), 1065-1076  
CODEN: CRSBW; ISSN: 0037-9026  
PB SGS  
DT Journal; \*\*\*General Review\*\*\*  
LA French  
AB A review with 35 refs. Apoptosis is a genetically programmed cell death that is required for morphogenesis during embryogenic development and for tissue homeostasis in adult organisms. In most cases, apoptosis involves cytochrome c release from mitochondria. In the cytosol, cytochrome c combines with APAF-1 in the presence of ATP to activate caspase-9 that, in turn, activates effector caspases such as caspase-3. Bcl-2 and related proteins control cytochrome c release from the mitochondria whereas IAP (for Inhibitor of Apoptosis) mols. modulate the activity of caspases. Plasma membrane receptors such as Fas (CD95, APO-1), characterized by a so-called "death domain" in their cytoplasmic domain, can activate the caspase cascade through adaptor mols. such as FADD (Fas-Associated protein with a Death Domain). Dysregulation of the apoptotic machinery plays a role in the pathogenesis of various diseases, and mols. involved in \*\*\*cell\*\*\* death pathways are potential \*\*\*therapeutic\*\*\* targets in immunol., \*\*\*neuro\*\*\*, cancer, infectious and inflammatory diseases.

- L10 ANSWER 5 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:55994 CAPLUS  
DN 130:265542  
TI Cellular and molecular basis of estrogen's  
\*\*\*neuroprotection\*\*\* :  
potential relevance for Alzheimer's disease  
AU Inestrosa, Nibaldo C.; Marzolo, Maria-Paz; Bonnefont, Andrea  
B.  
CS Departamento de Biología Celular y Molecular, Facultad de  
Ciencias,  
Pontificia Universidad Católica de Chile, Chile  
SO Mol. Neurobiol. (1998), 17(1-3), 73-86  
CODEN: MONBEW; ISSN: 0893-7648  
PB Humana Press Inc.  
DT Journal; \*\*\*General Review\*\*\*  
LA English  
AB A review, with 124 refs. Alzheimer's disease (AD) is one of the  
most  
common types of dementia among the aged population, with a  
higher  
prevalence in women. The reason for this latter observation  
remained  
unsolved for years, but recent studies have provided evidence that a  
lack  
of circulating estrogen in postmenopausal women could be a  
relevant  
factor. Moreover, follow-up studies among postmenopausal  
women who had  
received estrogen-replacement therapy (ERT), suggested that they  
had a  
markedly reduced risk of developing AD. In addn., studies among  
older  
women who already had AD indeed confirmed that a decrease in  
estrogen  
levels was likely to be an important factor in triggering the  
pathogenesis  
of the disease. In this review article, the authors will discuss the  
evidence suggesting that estrogen may have a protective role  
against AD,  
mainly through its action as: a trophic factor for cholinergic  
\*\*\*neurons\*\*\*, a modulator for the expression of  
apolipoprotein E (ApoE)  
in the brain, an antioxidant compd. decreasing the  
\*\*\*neuronal\*\*\*  
damage caused by oxidative stress, and a promoter of the physiol.  
nonamyloidogenic processing of the amyloid precursor protein  
(APP),  
decreasing the prodn. of the amyloid-beta-peptide (A-beta.), a key  
factor in the pathogenesis of AD.
- L10 ANSWER 6 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:52452 CAPLUS  
DN 130:280356  
TI Pathological immunoreactions of glial cells in Alzheimer's disease  
and  
possible sites of interference
- AU Schubert, P.; Ogata, T.; Miyazaki, H.; Marchini, C.; Ferroni, S.;  
Rudolphi, K.  
CS Department of Neuromorphology, Max Planck Institute for  
Neurobiology,  
Martinsried, Austria  
SO J. Neural Transm., Suppl. (1998), 54(Alzheimer's Disease: From  
Basic  
Research to Clinical Applications), 167-174  
CODEN: JNTSD4; ISSN: 0303-6995  
PB Springer-Verlag Wien  
DT Journal; \*\*\*General Review\*\*\*  
LA English  
AB A review with 29 refs. A significant role of a pathol. glial cell  
activation in the pathogenesis of Alzheimer's disease is supported  
by the  
growing evidence that inflammatory proteins, which are produced  
by  
reactive astrocytes, promote the transformation of diffuse  
beta-amyloid  
deposits into the filamentous, \*\*\*neurotoxic\*\*\* form. A no. of  
vicious circles, driven by the release of TNF-alpha. and free  
oxygen  
radicals from microglial cells, may cause an upregulated microglial  
activation and their prodn. of interleukin-1 which triggers,  
secondarily,  
the crucial activation of astrocytes. Reactive functional changes of  
glial cells seem to be controlled by an altered balance of the second  
messengers Ca2+ and cAMP and can be counterregulated by the  
endogenous  
cell modulator adenosine which strengthens the cAMP-dependent  
signaling  
chain. A further reinforcement of the homeostatic adenosine  
effects on  
glial cells by drugs, such as propentofylline, may add to  
\*\*\*neuroprotection\*\*\* in Alzheimer's disease.
- L10 ANSWER 7 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:39754 CAPLUS  
DN 130:261279  
TI Peripheral \*\*\*neuropathy\*\*\* with nucleoside antiretrovirals:  
Risk  
factors, incidence and management  
AU Moyle, Graeme J.; Sadler, Martin  
CS Kohler Clinic, Chelsea and Westminster Hospital, London, UK  
SO Drug Saf. (1998), 19(6), 481-494  
CODEN: DRSAAJ; ISSN: 0114-5916  
PB Adis International Ltd.  
DT Journal; \*\*\*General Review\*\*\*  
LA English  
AB A review with 67 refs. Distal sym. peripheral  
\*\*\*neuropathy\*\*\* is a  
common adverse experience in persons with HIV infection. This  
condition,  
which presents as a pain, numbness, burning and/or dysesthesia  
initially  
in the feet, is often multi-factorial in its origin. Nucleoside analog  
reverse transcriptase inhibitors represent an important contributor to
- peripheral \*\*\*neuropathy\*\*\*. Specifically, around 10% of  
patients  
receiving stavudine or zalcitabine and 1 to 2% of didanosine  
recipients  
may have to discontinue therapy with these agents due to  
\*\*\*neuropathy\*\*\*. Prompt withdrawal of these therapies  
enables gradual  
resoln. of signs and symptoms in most patients, although a period of  
symptom intensification may occur shortly after withdrawal. Risk  
factors  
for developing peripheral \*\*\*neuropathy\*\*\* during nucleoside  
analog  
\*\*\*therapy\*\*\* include low CD4+ \*\*\*cell\*\*\* count (<100  
cells/mm3), a  
prior history of an AIDS defining illness or neoplasm, a history of  
peripheral \*\*\*neuropathy\*\*\*, use of other \*\*\*neurotoxic\*\*\*  
agents  
including high alc. (ethanol) consumption and nutritional  
deficiencies  
such as low serum hydroxocobalamin levels. Thus, patients at  
increased  
risk of peripheral \*\*\*neuropathy\*\*\* should potentially avoid the  
use  
of the \*\*\*neurotoxic\*\*\* nucleoside analogs or be more carefully  
monitored during therapy. Management of this problem includes  
patient  
education, prompt withdrawal of the likely causative agent (giving  
consideration not to leave the patient on a sub-optimal therapy  
regimen)  
and simple analgesia, with augmentation with tricyclic  
antidepressants or  
anticonvulsant agents when pain is severe. New agents that may  
assist in  
managing this condition include levacocaine (acetyl-L-carnitine)  
and  
nerve growth factors such as recombinant human nerve growth  
factor.
- L10 ANSWER 8 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:20180 CAPLUS  
DN 130:205199  
TI Cellular delivery of \*\*\*neurotrophic\*\*\* factors as a potential  
treatment for Huntington's disease  
AU Emerich, Dwayne; Kordower, Jeffrey H.; Isaacson, Ole  
CS Department of Neuroscience, Alkermes, Inc., Cambridge, MA,  
USA  
SO CNS Regener. (1999), 477-502. Editor(s): Tuszynski, Mark H.;  
Kordower,  
Jeffrey H. Publisher: Academic, San Diego, Calif.  
CODEN: 67CYA3  
DT Conference; \*\*\*General Review\*\*\*  
LA English  
AB A review with approx. 100 refs. Huntington's Disease (HD) is a  
devastating  
\*\*\*neurodegenerative\*\*\* disorder with no effective treatments  
for the  
behavioral symptoms or the assoc. neural degeneration. In recent

years, the advent of appropriate animal models has permitted the evaluation of multiple therapeutic strategies. One of the more promising approaches currently under preclin. investigation and clin. consideration is the use of \*\*\*neurotrophic\*\*\* factors that might slow the progression or even prevent the onset of the behavioral and pathol. consequences of HD. This chapter highlights the use of transplanted genetically modified cells as a means of delivering \*\*\*neurotrophic\*\*\* factors. Studies in both rodent and nonhuman primate models of HD suggest that trophic factors such as NGF and CNTF exert marked \*\*\*neuroprotective\*\*\* effects upon the vulnerable striatal \*\*\*neurons\*\*\* that degenerate in HD. Although the mechanisms by which these factors exert their beneficial effects remain unclear, their clearest potency in both rodent and primate models of HD provide the hope that a means of preventing or slowing the relentlessly progressive motor and cognitive declines in HD may be forthcoming. Furthermore, excitotoxicity has been implicated in a variety of pathol. conditions including ischemia, and \*\*\*neurodegenerative\*\*\* diseases such as Huntington's, Parkinson's, and Alzheimer's. Accordingly, delivered \*\*\*neurotrophic\*\*\* factors may provide one means of preventing the cell loss and assoc. behavioral abnormalities of these and possibly other human disorders.

L10 ANSWER 9 OF 66 CAPLUS COPYR(IGHT) 1999 ACS  
AN 1999:20171 CAPLUS

DN 130:245945  
T1 Neural stem cell lines for CNS repair  
AU Martinez-Serrano, Alberto; Snyder, Evan Y.  
CS Center of Molecular Biology "Severo Ochoa", Autonomous University of Madrid-CSIC, Madrid, Spain  
SO CNS Regener. (1999), 203-250. Editor(s): Tuszynski, Mark H., Kordower, Jeffrey H. Publisher: Academic, San Diego, Calif.  
CODEN: 67CYA3  
DT Conference; \*\*\*General Review\*\*\*  
LA English  
AB A review with 112 refs. The establishment and use of stable, engraftable, clonal, multipotent neural stem cell lines have recently added an exciting

new dimension to strategies for cell replacement and gene transfer to the diseased mammalian CNS. These neural stem cell clones can serve as convenient, well-controlled models for the in vivo study of CNS development and regeneration, can constitute readily available, well-characterized, safe sources of graft material for the replacement of multiple types of degenerated neural cells, and can provide excellent vehicles for the transfer of genes encoding diffusible and non-diffusible factors directly to the CNS. By exploiting their basic biol. properties, these cells are able to bypass restrictions imposed by the blood-brain barrier to deliver therapeutic gene products in a sustained, direct, and perhaps regulated fashion throughout the CNS (either because they intrinsically produce these substances or because they have been genetically engineered ex vivo to do so). Furthermore, although they may disseminate these gene products throughout the brain, they nevertheless restrict that distribution to only the CNS. In addn., they may replace dysfunctional neural cells in both a site-specific and more global manner (circumventing the concern that in many alternative gene transfer techniques "new" genetic information is supplied to "old" neural circuits, many of which may have degenerated). Neural stem cell clones may be used for \*\*\*neurodegenerative\*\*\* conditions that occur both during development and in the mature brain. In fact, they appear to be capable of altering their migration and differentiation in response to certain as yet unspecified signals elaborated during active \*\*\*neurodegeneration\*\*\*. Thus, these vehicles may overcome many of the limitations of viral and non-neural cellular vectors, as well as pharmacol. and genetic interventions. A growing body of evidence has, indeed, affirmed the efficacy of a neural stem cell-based strategy for the replacement of defective or absent genes and cells, and has suggested that re-population of the diseased or injured CNS with such cells may promote both anatomical and behavioral recovery in animal models of \*\*\*neurodegenerative\*\*\* conditions. These recent expts. with clones of rodent neural progenitor and stem cells are bringing us rapidly closer to the challenge of repairing the CNS in genuine clin. settings using similarly well-characterized, fully controlled, multifaceted cellular tools of

human origin.

L10 ANSWER 10 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:20170 CAPLUS

DN 130:245944  
T1 The use of neural progenitor \*\*\*cells\*\*\* for \*\*\*therapy\*\*\* in the CNS disorders  
AU Ray, Jasodhara, Palmer, Theo D.; Shihabuddin, Larnya S.; Gage, Fred H.  
CS Laboratory of Genetics, Salk Institute, La Jolla, CA, USA  
SO CNS Regener. (1999), 183-201. Editor(s): Tuszynski, Mark H., Kordower, Jeffrey H. Publisher: Academic, San Diego, Calif.  
CODEN: 67CYA3  
DT Conference; \*\*\*General Review\*\*\*  
LA English  
AB A review with 84 refs. In recent years a significant no. of \*\*\*neuro\*\*\* diseases have been defined at the mol. level. Somatic gene \*\*\*therapy\*\*\* using genetically modified non-\*\*\*neural\*\*\* \*\*\*cells\*\*\* expressing \*\*\*therapeutic\*\*\* factors have been successfully used in animal models of \*\*\*neurodegenerative\*\*\* diseases. Ability to grow central nervous system (CNS)-derived neural progenitor cells has proven to be extremely useful to study a diverse phenomenon including the fate choice, differentiation, and synaptic maturation of cells. Immortal or perpetual cultures of neural progenitor cells implanted into the rodent brain survive, migrate, and integrate in the host cytoarchitecture. These cells can be genetically modified to express therapeutic gene products. The ability of the implanted cells to integrate in the host brain and express transgene products in situ offer potential approaches for gene therapy in certain CNS diseases. The utility of this approach has already been explored in animal models of \*\*\*neurodegenerative\*\*\* diseases. This chapter reviews the recent advances made in understanding the nature and potentiality of neural progenitor cells in vitro and in vivo as well as their possible use for \*\*\*cell\*\*\* replacement and gene \*\*\*therapy\*\*\*.

=> d 11-20 bib ab

L10 ANSWER 11 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1999:17041 CAPLUS  
DN 130:177630

TI A commentary on glial cell line-derived \*\*\*neurotrophic\*\*\* factor (GDNF): from a glial secreted molecule to gene therapy  
 AU Bohn, Martha C.  
 CS Children's Memorial Institute for Education and Research, Northwestern  
 University Medical School, Chicago, IL, 60614, USA  
 SO Biochem Pharmacol. (1999), 57(2), 135-142  
 CODEN: BCPA6; ISSN: 0006-2952  
 DT Journal; \*\*\*General Review\*\*\*  
 LA English  
 AB A review, with 72 refs. Glial cell line-derived \*\*\*neurotrophic\*\*\* factor (GDNF) was identified as a consequence of the hypothesis that glia secrete factors that influence growth and differentiation of specific classes of \*\*\*neurons\*\*\*. Glia are a likely source of adnl. \*\*\*neurotrophic\*\*\* factors; however, this strategy has not been applied extensively. The discovery of GDNF in 1993 led to an abundance of studies that within only a few years qualified GDNF as a bona fide \*\*\*neurotrophic\*\*\* factor. Of particular interest are studies demonstrating the effectiveness of GDNF protein in ameliorating \*\*\*neurodegeneration\*\*\* in animal models of Parkinson's disease and anyotrophic lateral sclerosis (ALS). It remains to be detd. whether GDNF will be an effective therapy in humans with these diseases. However, since these diseases are slowly progressive and the CNS relatively inaccessible, the delivery of GDNF as a therapeutic mol. to the CNS in a chronic manner is problematic. Studies addressing this problem are applying viral vector mediated transfer of the GDNF gene to the CNS in order to deliver biosynthesized GDNF to a specific location in a chronic manner. Recent studies suggest that these GDNF gene therapy approaches are effective in rat models of Parkinson's disease. These studies are reviewed in the context of what developments will be needed in order to apply GDNF gene therapy to the clinic.

L10 ANSWER 12 OF 66 CAPLUS COPYRIGHT 1999 ACS  
 AN 1999:10481 CAPLUS  
 DN 130:221120  
 TI \*\*\*Neuronal\*\*\* cell death mechanism in glaucomatous optic \*\*\*neuropathy\*\*\*  
 AU Murakami, Akira; Okisaka, Shigekuni  
 CS Department of Ophthalmology, National Defence Medical College, Japan  
 SO Nippon Ganka Gakkai Zasshi (1998), 102(10), 645-653  
 CODEN: NGZAA6; ISSN: 0029-0203  
 PB Nippon Ganka Gakkai

DT Journal; \*\*\*General Review\*\*\*  
 LA Japanese  
 AB A review with 85 refs. Apoptosis of retinal ganglion cells has been obsd. in exptl. glaucomatous models and human glaucomatous eyes in recent pathol. studies. It seems that retinal ganglion cells in glaucomatous optic \*\*\*neuropathy\*\*\* die by a process similar to programmed cell death. Deprivation of \*\*\*neurotrophic\*\*\* factors, ischemia, chronic elevation of glutamate, and disorganized NO metab. are suspected to be factors affecting \*\*\*neuronal\*\*\* loss in glaucoma, and most of these factors are known to activate the mechanism of cellular suicidal death. One of the common switches for the death mechanism seems to be in the mitochondria and to be controlled by Bcl-2 family proteins. A major goal of \*\*\*neuronal\*\*\* cell death research in glaucomatous \*\*\*neuropathy\*\*\* is to identify its mol. components and mechanisms of regulation. This information will lead to \*\*\*therapeutic\*\*\* agents that can modulate the \*\*\*cell\*\*\* death process in the treatment of glaucomatous \*\*\*neuropathy\*\*\*.

L10 ANSWER 13 OF 66 CAPLUS COPYRIGHT 1999 ACS  
 AN 1998:802182 CAPLUS  
 DN 130:207923  
 TI Calcium and cellular death  
 AU Sattler, Rita; Tymianski, Michael  
 CS Playfair Neuroscience Unit, The Toronto Hospital Research Institute, Toronto, ON, Can.  
 SO Integr. Aspects Calcium Signalling (1998), 267-290. Editor(s): Verkhratsky, Alexej Nestorovich; Toescu, Emil C. Publisher: Plenum, New York, N. Y.  
 CODEN: 67AWAL  
 DT Conference; \*\*\*General Review\*\*\*  
 LA English  
 AB A review, with many refs. Recent years have seen significant advances in our conceptualization of mechanisms by which Ca2+ ions may mediate cell death. In spite of the complexities assoc. with \*\*\*neuronal\*\*\* Ca2+ homeostasis, it appears that \*\*\*neurons\*\*\* possess a powerful machinery for dealing with Ca2+ excess. Thus, "Ca2+ excess", conceptualized as an unusually large cellular Ca2+ load, is in itself insufficient to cause \*\*\*neurotoxicity\*\*\*. Instead, the relationship between Ca2+ influx and \*\*\*neurotoxicity\*\*\* is significantly

more complex, as it depends not only on the quantity of Ca2+ which enters the cell, but also on the subcellular compartments to which Ca2+ ions gain access. This feature of Ca2+ \*\*\*neurotoxicity\*\*\* can be measured both using total Ca2+ flux measurements with radiolabeled Ca2+ ions, or using fluorescent free Ca2+ indicators. However, Ca2+ ion fluxes must be meticulously restricted to distinct influx pathways for the dependence of Ca2+ \*\*\*neurotoxicity\*\*\* on a given subcellular location of Ca2+ ions to be reliably inferred. The corollary of these recent observations is that " \*\*\*neurotoxic\*\*\* " Ca2+ ions must trigger specific signaling cascades for \*\*\*neurotoxicity\*\*\* to occur, since such cascades do not appear to be triggered when Ca2+ ions enter cells through "non toxic" pathways. Thus, the mol. substrates governing toxic signaling pathways must also be compartmentalized with toxic Ca2+ fluxes. In many \*\*\*neurons\*\*\*, toxic Ca2+ entry occurs through NMDA receptors which are implicated in numerous physiol. functions. Therefore, it is likely that mol. substrates which participate in toxic phenomena also subserve physiol. roles under less stressful conditions. This raises the likelihood that, rather than being caused by a non-specific disruption of the cell's homeostatic machinery, Ca2+ \*\*\*neurotoxicity\*\*\* is a pathol. extension of physiol. Ca2+ signaling. Thus, future research must be aimed at revealing the specific signal transduction pathways involved in Ca2+ \*\*\*neurotoxicity\*\*\*, and at identifying mol. targets whose pharmacol. or genetic manipulation might produce improved \*\*\*therapies\*\*\* for Ca-mediated \*\*\*cell\*\*\* death.

L10 ANSWER 14 OF 66 CAPLUS COPYRIGHT 1999 ACS  
 AN 1998:798523 CAPLUS  
 DN 130:148113  
 TI Telomeres and telomerase: targets for cancer chemotherapy?  
 AU Perry, Philip J.; Kelland, Lloyd R.  
 CS Cancer Research Campaign Biomolecular Structure Unit and Centre for Cancer Therapeutics, The Institute of Cancer Research, Surrey, SM2 5NG, UK  
 SO Expert Opin. Ther. Pat. (1998), 8(12), 1567-1586  
 CODEN: EOTPEG; ISSN: 1354-3776  
 PB Ashley Publications  
 DT Journal; \*\*\*General Review\*\*\*  
 LA English



AB A review with 141 refs. Telomerase is a specialised ribonucleoprotein comprising of, at present, 3 known components: the human telomerase RNA component (hTR); the human telomerase reverse transcriptase catalytic subunit (hTERT), and TP1, a telomerase-associated protein. Applications involving telomerase have been proposed in the fields of \*\*\*cellular\*\*\* engineering, diagnostics/prognostics and \*\*\*therapeutics\*\*\*. In the diagnostics area, around 85% of human cancers have been shown to possess telomerase activity, while such activity is not detectable in most somatic cells. In some cases (notably \*\*\*neuroblastomas\*\*\*, gastric and breast tumors), higher levels of telomerase activity were associated with poor prognosis. Telomerase activity, which has generally been measured using a highly sensitive PCR-based TRAP assay, may also be assessed to monitor residual disease following surgery and/or chemotherapy. As telomerase appears to be selectively expressed in tumors vs. normal cells, many have proposed that the enzyme represents a good target for inhibition. Efforts are underway to target various components of the telomerase/telomere machinery including the hTR template region using antisense oligonucleotides and peptide nucleic acids (PNAs), some of which inhibit at the nanomolar level, hTERT, and the telomerase/telomerase interaction. Small-mol. inhibitors of telomerase have recently been described. These include a series of regioisomeric diamidoanthracene-9,10-diones (the best of which inhibit telomerase in cell-free assays with IC50 values of 1 - 5 .mu.M) and porphyrin-based mols. These mols. have been proposed to act via stabilization of guanine-quadruplexes, structures associated with telomeres and telomerase. Reverse transcriptase inhibitors, such as AZT triphosphate, have also been shown to inhibit telomerase. This will clearly be an area where, in the near future, potent inhibitors will be developed thus permitting further target validation experiments to be performed in tumor-bearing mice and ultimately in cancer patients.

L10 ANSWER 15 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1998:787844 CAPLUS

DN 130:191238  
TI Approaches in treating nerve cell death with calcium chelators  
AU Tymianski, Michael  
CS Neuroprotection Laboratory, Playfair Neuroscience Unit, Toronto Hospital, Toronto, ON, Can.  
SO Cell Death Dis. Nerv. Syst. (1999), 609-631. Editor(s): Koliatsos, Vassilis E.; Ratan, Rajiv R. Publisher: Humana, Totowa, N. J. CODEN: 67ARAG  
DT Conference; \*\*\*General Review\*\*\*  
LA English  
AB A review, with 137 refs., discussing current knowledge on the role of Ca<sup>2+</sup> buffers as probes of mechanisms leading to nerve \*\*\*cell\*\*\* death and as potential \*\*\*therapeutic\*\*\* agent for Ca<sup>2+</sup>-dependent \*\*\*neurotoxicity\*\*\*.

L10 ANSWER 16 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1998:787842 CAPLUS  
DN 130:163259  
TI Tropic factors as therapeutic agents for diseases characterized by \*\*\*neuronal\*\*\* death  
AU Koliatsos, Vassilis E.; Mochetti, Italo  
CS Departments of Pathology (Neuropathology), Neurology, Neuroscience, and Psychiatry and Behavioral Science, The Johns Hopkins University School of Medicine, Baltimore, MD, USA  
SO Cell Death Dis. Nerv. Syst. (1999), 545-591. Editor(s): Vassilis E.; Ratan, Rajiv R. Publisher: Humana, Totowa, N. J. CODEN: 67ARAG  
DT Conference; \*\*\*General Review\*\*\*  
LA English  
AB A review with 305 refs. with the following key sections: trophic factors as biol. \*\*\*therapies\*\*\*; \*\*\*neuronal\*\*\* \*\*\*cell\*\*\* death as a \*\*\*therapeutic\*\*\* target (distal and proximal interventions); \*\*\*neurobiol\*\*\* of trophic peptides; novel concepts in the \*\*\*neurobiol\*\*\* of trophic factors; activity-related changes in trophic factor expression and utilization; challenges in the clin. pharmacol. of trophic factors; and conclusions.

L10 ANSWER 17 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1998:704109 CAPLUS  
DN 130:90564  
TI Retinal regeneration mechanism and application towards congenital retinal diseases therapy  
AU Tomita, Hiroshi; Abe, Toshiaki; Tamoi, Makoto  
CS Medical School, Tohoku University, Japan

SO Rinsho Kagaku (Osaka) (1998), 34(9), 1276-1282  
CODEN: RIKAER, ISSN: 0385-0323  
PB Esuto K. K.  
DT Journal; \*\*\*General Review\*\*\*  
LA Japanese  
AB A review with 13 refs., on history of retina regeneration, retinal pigment epithelial cell differentiation in retina regeneration, retina regeneration from neural precursor cells; mol. mechanism of retina regeneration; and therapy of congenital retinal diseases by \*\*\*neuroretina\*\*\* regeneration, gene \*\*\*therapy\*\*\*, retina \*\*\*cell\*\*\* transplant, and \*\*\*neurotrophic\*\*\* and growth factors.

L10 ANSWER 18 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1998:582020 CAPLUS  
DN 129:339341  
TI Gemcitabine and paclitaxel combinations in non-small-cell lung cancer  
AU Dombrowsky, Per, Giaccone, Giuseppe; Sandier, Alan, Schwartzmann, Gilberto  
CS Department of Oncology, Herlev Hospital, Herlev, DK 2730, Den.  
SO Semin. Oncol. (1998), 25(4, Suppl. 9), 44-50  
CODEN: SOLGAV; ISSN: 0093-7754  
PB W. B. Saunders Co.  
DT Journal; \*\*\*General Review\*\*\*  
LA English  
AB A review with 44 refs. Gemcitabine and paclitaxel are new cytotoxic agents that have been used both as single agents and in combination, particularly with cisplatin, in the \*\*\*therapy\*\*\* of non-small-cell lung cancer (NSCLC) with promising results. The lack of overlapping toxicities and different mechanisms of action of gemcitabine and paclitaxel make the combination of these drugs appealing in the treatment of NSCLC. A no. of phase I and II trials are evaluating the use of this combination of cytotoxic agents as 1st-line therapy and as 2nd-line therapy in patients with advanced NSCLC. In ongoing phase II trials using a 21-day schedule, the combination of gemcitabine and paclitaxel therapy appears to be well-tolerated, with response rates ranging 29%-58% and hematol. toxicities that are mild to moderate in severity. Other reported toxicities included alopecia, fatigue, and flu-like symptoms, which were also mild to moderate. However, grade 2/3 \*\*\*neurotoxicity\*\*\* was also reported. In conclusion, preliminary results from these early phase II trials of gemcitabine/paclitaxel combination therapy in advanced NSCLC

are encouraging

L10 ANSWER 19 OF 66 CAPLUS COPYRIGHT 1999 ACS  
AN 1998:412985 CAPLUS

DN 129:134324

TI \*\*\*Cellular\*\*\* \*\*\*therapeutic\*\*\* approaches for

\*\*\*neurodegenerative\*\*\* disorders

AU Sanberg, Paul R.; Willing, Alison E.

CS Div. Neurosurgery & Neurosci. Progr., University of South  
Florida, Tampa,

FL, 33612, USA

SO Nucleic Acids Symp. Ser. (1998), 38(Advances in Gene

Technology: Molecular

Biology in the Conquest of Disease), 139-142

CODEN: NACSD8; ISSN: 0261-3166

PB Oxford University Press

DT Journal; \*\*\*General Review\*\*\*

LA English

AB A review, with 37 refs. Topics discussed include: cellular  
transplantation in Parkinson's disease; fetal tissue transplantation;  
xenografts of fetal tissue; alternate sources of dopaminergic cells;  
issues of graft rejection; enhancing graft survival with growth  
factors.

Sertoli cells and Parkinson's disease; cell transplantation in  
Huntington's disease; and transplantation in stroke models.

L10 ANSWER 20 OF 66 CAPLUS COPYRIGHT 1999 ACS

AN 1998:322517 CAPLUS

DN 129:75851

TI Adenosine A2B receptors: a novel therapeutic target in asthma?

AU Feoktistov, Igor; Polosa, Riccardo; Holgate, Stephen T.;

Biaggiotti, Italo

CS Div. Cardiol., Vanderbilt Univ., Nashville, TN, 37232-2195,

USA

SO Trends Pharmacol. Sci. (1998), 19(4), 148-153

CODEN: TPHSDY; ISSN: 0165-6147

PB Elsevier Science Ltd

DT Journal; \*\*\*General Review\*\*\*

LA English

AB A review with 67 refs. Adenosine is an endogenous nucleoside  
that

modulates many physiol. processes. Its actions are mediated by  
interaction with specific cell membrane receptors. Four subtypes of  
adenosine receptor have been cloned: A1, A2A, A2B and A3.

Significant

advancement has been made in our understanding of the mol.  
pharmacol. and

physiol. relevance of adenosine receptors but our knowledge of

A2B

receptors lags behind that of other receptor types. Only recently

have

potentially important functions been discovered for the A2B

receptors,

prompting a renewed interest in this receptor types. A2B receptors

have

been implicated in the regulation of vascular smooth muscle tone,

cell

growth, intestinal function and \*\*\*neurosecretion\*\*\*. In this  
review,

the authors focus on the role of A2B receptors in mast cell

activation and

the potential relevance of this action on asthma.

=> file medline

COST IN U.S. DOLLARS SINCE FILE TOTAL

ENTRY SESSION 86.54 86.69

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL

ENTRY SESSION -16.60 -16.60

CA SUBSCRIBER PRICE

FILE 'MEDLINE' ENTERED AT 09:30:39 ON 20 SEP 1999

FILE LAST UPDATED: 13 SEP 1999 (19990913/UP). FILE

COVERS 1960 TO DATE.

MEDLINE has been reloaded to reflect the annual MeSH changes  
made by  
the National Library of Medicine for 1999. Enter HELP RLOAD for  
details.

OLDMEDLINE, data from 1960 through 1965 from the Cumulated  
Index  
Medicus (CIM), has been added to MEDLINE. See HELP  
CONTENT for details.

Left, right, and simultaneous left and right truncation are available in  
the  
Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY  
AND ACCURATE  
SUBSTANCE IDENTIFICATION.

FILE 'MEDLINE' ENTERED AT 09:30:39 ON 20 SEP 1999

=> s 110

<-----User Break----->

u

SEARCH ENDED BY USER

=> s 19

'AB' IS NOT A VALID FIELD CODE

1853952 CELL?

0 (THERAPY)AB

1849421 (THERAPY)BI

11352 (CELL)?(SA)(THERAPY)AB.BI

0 NEURO?/AB

620325 NEURO?/BI

L11 559 L2 AND NEURO?/AB.BI

=> s 111 and (unpredict? or problem?)/ab,bi

'AB' IS NOT A VALID FIELD CODE

0 UNPREDICT?/AB

4788 UNPREDICT?/BI

0 PROBLEM?/AB

291782 PROBLEM?/BI

L12 28 L11 AND (UNPREDICT? OR PROBLEM?)/AB.BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 28 ANSWERS -  
CONTINUE? Y/(N)y

L12 ANSWER 1 OF 28 MEDLINE

AN 1999360700 MEDLINE

DN 99360700

TI Convection-enhanced selective excitotoxic ablation of the  
\*\*\*neurons\*\*\*  
of the globus pallidus internus for treatment of parkinsonism in  
nonhuman  
primates

AU Lonser R R; Corthesy M E; Morrison P F; Gogate N; Oldfield E

H

CS Surgical Neurology Branch, National Institute of Neurological

Disorders

National

Stroke, and Bioengineering and Physical Science Program,

Institutes of Health, Bethesda, Maryland 20892-1414, USA.

SO JOURNAL OF NEUROSURGERY, (1999 Aug) 91 (2) 294-302.

Journal code: JD3. ISSN: 0022-3085.

CY United States

DT Journal; Article, (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals; Cancer

Journals

EM 199910

EW 19991003

AB OBJECT: Selective treatment of central nervous system (CNS)  
structures

holds therapeutic promise for many \*\*\*neurological\*\*\*

disorders,

including Parkinson's disease (PD). The ability to inhibit or

augment

specific \*\*\*neuronal\*\*\* populations within the CNS reliably by

using

present therapeutic techniques is limited. To overcome this

\*\*\*problem\*\*\*, the authors modeled and developed a method

in which

convection was used to deliver compounds to deep brain nuclei in a

reproducible, homogeneous, and targeted manner. To determine the

feasibility and clinical efficacy of convective drug delivery for treatment of a \*\*\*neurological\*\*\* disorder, the investigators selectively ablated globus pallidus internus (GPi) \*\*\*neurons\*\*\* with quinolinic acid (QA), an excitotoxin, in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced model of primate parkinsonism. METHODS: After the parameters of convective distribution to the GPi were confirmed by infusion of biotinylated albumin into the GPi of a primate (Macaca mulatta), seven adult monkeys of this species were rendered either fully parkinsonian by intravenous injections of MPTP (five animals) or hemiparkinsonian by a right-sided intracarotid injection of this agent (two monkeys). Using convection-enhanced delivery to the GPi, animals were infused with either QA (three fully parkinsonian, two hemiparkinsonian) or saline (two fully parkinsonian). The three fully parkinsonian animals that underwent GPI lesioning with QA had substantial improvement of PD symptoms, manifested by a marked increase in activity (34 +/- 2.5%; mean +/- standard deviation) and dramatic improvement of parkinsonian clinical scores. In contrast, the control animals did not improve (activity monitor change = -1.5 +/- 0.5%). The two hemiparkinsonian animals that underwent QA lesioning of the GPi had dramatic recovery of extremity use. Histological examination revealed selective neural ablation of GPi \*\*\*neurons\*\*\* (mean loss 87%) with sparing of surrounding gray and white matter structures. No animal developed worsening signs of PD or \*\*\*neurological\*\*\* deficits after infusion. CONCLUSIONS: Convection-enhanced delivery of QA permits selective, region-specific (GPi), and safe lesioning of \*\*\*neural\*\*\* subpopulations, resulting in dramatic improvement in parkinsonian symptomatology. The properties of convection-enhanced delivery indicate that this method could be used for chemical \*\*\*neurosurgery\*\*\* for medically refractory PD and that it may be ideal for \*\*\*cell\*\*\*-specific \*\*\*therapeutic\*\*\* ablation or trophic treatment of other targeted structures associated with CNS disorders.

L12 ANSWER 2 OF 28 MEDLINE  
AN 1999242345 MEDLINE  
DN 99242345

TI Leukocytopheresis therapy by extracorporeal circulation using a leukocyte removal filter [editorial].  
AU Suemitsu J, Yoshida M, Yamawaki N, Yamashita Y  
SO Ther Apher, (1998 Feb) 2 (1) 31-6. Ref: 12  
Journal code: DBB. ISSN: 1091-6660.  
CY United States  
DT Editorial  
General Review, (REVIEW) (REVIEW, TUTORIAL)  
LA English  
FS Priority Journals  
EM 199907  
EW 19990703  
AB Leukocytopheresis therapy has been used to try to treat such intractable diseases as autoimmune and \*\*\*neurologic\*\*\* diseases, achieving good results. However, a number of \*\*\*problems\*\*\* have been identified in leukocyte removal by thoracic duct drainage or continuous centrifugal separation, namely the high risk, expensive cost, and complicated operation. Asahi Medical Co. has developed an innovative solution for such conventional \*\*\*problems\*\*\*. Its new leukocyte removal filter (Cellsorba) is capable of removing white blood cells by perfusion of whole blood by means of simple extracorporeal circulation. Leukocytopheresis \*\*\*therapy\*\*\* using the \*\*\*Cellsorba\*\*\* column is being confirmed as extremely effective for many inflammatory diseases, as well as in autoimmune and \*\*\*neurologic\*\*\* diseases. This paper outlines information about the Cellsorba column and introduces several reports on therapeutic results.

L12 ANSWER 3 OF 28 MEDLINE  
AN 1999094700 MEDLINE  
DN 99094700  
TI Peripheral \*\*\*neuropathy\*\*\* with nucleoside antiretrovirals: risk factors, incidence and management.  
AU Moyle G J, Sadler M  
CS Koblitz Clinic, Chelsea and Westminster Hospital, London, England.  
SO DRUG SAFETY, (1998 Dec) 19 (6) 481-94. Ref: 67  
Journal code: AHQ. ISSN: 0114-5916.  
CY New Zealand  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review, (REVIEW) (REVIEW LITERATURE)  
LA English  
FS Priority Journals  
EM 199906  
EW 19990603

AB Distal symmetrical peripheral \*\*\*neuropathy\*\*\* is a common adverse experience in persons with HIV infection. This condition, which presents as a pain, numbness, burning and/or dysaesthesia initially in the feet, is often multi-factorial in its origin. Nucleoside analogue reverse transcriptase inhibitors represent an important contributor to peripheral \*\*\*neuropathy\*\*\*. Specifically, around 10% of patients receiving stavudine or zalcitabine and 1 to 2% of didanosine recipients may have to discontinue therapy with these agents due to \*\*\*neuropathy\*\*\*. Prompt withdrawal of these therapies enables gradual resolution of signs and symptoms in most patients, although a period of symptom intensification may occur shortly after withdrawal. Risk factors for developing peripheral \*\*\*neuropathy\*\*\* during nucleoside analogue \*\*\*therapy\*\*\* include low CD4+ \*\*\*cell\*\*\* count (<100 cells/mm3), a prior history of an AIDS defining illness or neoplasm, a history of peripheral \*\*\*neuropathy\*\*\*, use of other \*\*\*neurotoxic\*\*\* agents including high alcohol (ethanol) consumption and nutritional deficiencies such as low serum hydroxocobalamin levels. Thus, patients at increased risk of peripheral \*\*\*neuropathy\*\*\* should potentially avoid the use of the \*\*\*neurotoxic\*\*\* nucleoside analogues or be more carefully monitored during therapy. Management of this \*\*\*problem\*\*\* includes patient education, prompt withdrawal of the likely causative agent (giving consideration not to leave the patient on a sub-optimal therapy regimen) and simple analgesia, with augmentation with tricyclic antidepressants or anticonvulsant agents when pain is severe. New agents that may assist in managing this condition include levacarnine (acetyl-L-carnitine) and nerve growth factors such as recombinant human nerve growth factor.

L12 ANSWER 4 OF 28 MEDLINE  
AN 1999081926 MEDLINE  
DN 99081926  
TI Use of gene marking technologies in oncology.  
AU Brenner M  
CS Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, Texas 77030, USA.

SO FORUM, (1998 Oct-Dec) 8 (4) 342-53. Ref: 67  
Journal code: C0R. ISSN: 1121-8142.

CY Italy  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LA English  
EM 199904  
EW 19990401

AB Investigation of the mechanism of relapse in patients receiving stem

\*\*\*cell\*\*\* rescue as \*\*\*therapy\*\*\* for malignant disease has been facilitated by gene marking studies. These studies have shown the marker

gene to be present in malignant cells in the patient at the time of relapse, indicating that infused stem cells can contribute to disease recurrence. As normal progenitor cells are also marked and can be tracked in vivo, these studies have also helped us learn how haemopoietic stem cells respond to manipulation, for example with growth factors.

Second generation studies with multiple, modified vectors are beginning to provide information about a wider variety of clinical and biological issues, including the efficacy of purging. Although marker studies have been useful for haematological malignancy and for

\*\*\*neuroblastoma\*\*\*, they are hampered by the low efficiency of marking achieved by retroviral vectors. For many malignancies, marking efficiencies are insufficient for useful information to be obtained. This \*\*\*problem\*\*\* may be overcome by the introduction of vectors that, unlike retroviruses, can stably integrate in cells that are not in cycle at the time of vector exposure.

Other improvements will focus on the marker genes themselves, using marker elements that are simpler to track and will not produce any modification of the cells' behaviour. Finally, marker studies have proved safe so far, but follow-up of the treated patients continues.

L12 ANSWER 5 OF 28 MEDLINE  
AN 1999051537 MEDLINE  
DN 99051537

TI [Promoting remyelination as a future therapeutic principle in multiple sclerosis?].

Remyelinisierungsforderung als zukunftiges Therapieprinzip der Multiplen Sklerose?

AU Pohlau D, Aktas O, Epplen C, Hartung H P, Hoffmann V, Pruntek H  
CS Neurologische Klinik, Ruhr-Universität Bochum am St. Josef

Hospital.

SO NERVENARZT, (1998 Oct) 69 (10) 841-50. Ref: 112  
Journal code: NWS. ISSN: 0028-2804.

CY GERMANY: Germany, Federal Republic of  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LA German  
FS Priority Journals  
EM 199904  
EW 19990402

AB Multiple sclerosis (MS), the most common \*\*\*neurological\*\*\* autoimmune disorder diagnosed in young adults, is characterised by the repeated occurrence of demyelinating lesions within the central nervous system

(CNS). Promotion of remyelination in the brain and spinal cord constitutes a potential strategy for therapeutic intervention in MS and other demyelinating diseases. Three different principles are known to promote remyelination in the CNS of different animal models: Application of growth factors, transplantation of myelin-forming \*\*\*cells\*\*\* and intravenous immunoglobulin (IVIg) \*\*\*therapy\*\*\*. However, the systemic application of growth factors could be limited by effects on unaffected tissue.

For successful transplantation we still have the \*\*\*problem\*\*\* of homologous cells not tolerated by an immunological different organism.

Currently the required combination of growth factors needed to cultivate human homologous cells is not known, so that cells suitable for transplantation are still not available. Nevertheless, there is increasing evidence for beneficial effects of IVIg therapy on the promotion of remyelination in humans. In this review we summarise recent findings on the regulation of myelin sheath development and oligodendrocyte differentiation, and discuss the presented strategies in the context of possible clinical application for the therapy of MS.

L12 ANSWER 6 OF 28 MEDLINE  
AN 1998430737 MEDLINE  
DN 98430737

TI Transduced fibroblasts and metachromatic leukodystrophy lymphocytes

transfer arylsulphatase A to myelinating glia and deficient cells in vitro.

AU Sangalli A, Taveggia C, Salvati A, Wrabetz L, Bordignon C, Severini G M  
CS Department of Biology and Genetics, University of Verona, Italy.  
SO HUMAN GENE THERAPY, (1998 Sep 20) 9 (14) 2111-9.

Journal code: A12. ISSN: 1043-0342.  
CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English  
FS Priority Journals  
EM 199902  
EW 19990204

AB Metachromatic leukodystrophy (MLD) is a lysosomal storage disease, caused by deficiency of arylsulphatase A (ASA), that manifests primarily in the

white matter of the nervous system. Currently, no specific treatment exists that will reverse its fatal outcome. Replacement therapy has been hampered by the blood-brain barrier (BBB). To circumvent this \*\*\*problem\*\*\* we designed an ex vivo gene therapy strategy that includes the retrovirus-mediated ASA transduction of cells, such as activated lymphocytes, that are able to traverse the BBB or other membranes of the CNS. For this purpose, two recombinant retroviruses based on the pLXSN vector were produced, containing the wild-type ASA cDNA or a pseudodeficiency ASA cDNA, which encodes a smaller enzyme activity. After transduction, ASA activity increased more than 100-fold in fibroblasts from an MLD patient. Furthermore, ASA-transduced MLD PBLs expressed 30 times higher ASA activity when compared with control PBLs.

Moreover, cell culture experiments demonstrated that transduced fibroblasts could efficiently transfer ASA to deficient cells across a transwell barrier, whereas transduced MLD lymphocytes could transfer ASA to deficient fibroblasts only by direct cell-to-cell contact. Finally, ASA was taken up by normal oligodendrocytes and Schwann cells, the target myelinating glial \*\*\*cells\*\*\* for \*\*\*therapy\*\*\* in MLD. These data suggest possible short-term strategies for transfer of ASA into the CNS via transduced autologous cells while long-term strategies, related to autologous transduced bone marrow transplant, take effect in patients.

L12 ANSWER 7 OF 28 MEDLINE  
AN 1998043387 MEDLINE  
DN 98043387

TI Lack of immune responses to immediate or delayed implanted allogeneic and xenogeneic Schwann cell suspensions.

AU Hermanns S, Wunderlich G, Rosenbaum C, Hanemann C O, Müller H W, Stichel C  
CS Molecular Neurobiology Laboratory, Department of Neurology,

Dusseldorf,  
Germany.

SO GLA, (1997 Nov) 21 (3) 299-314.  
Journal code: GLI. ISSN: 0894-1491.

CY United States  
DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199802

EW 19980204

AB Previous studies have shown that Schwann \*\*\*cell\*\*\*  
implantation

offers a potential \*\*\*therapeutic\*\*\* approach to a variety of  
\*\*\*neurodegenerative\*\*\* disorders and traumatic injuries. In a  
clinically relevant paradigm, however, the implantation of  
autologous

Schwann cells is \*\*\*problematic\*\*\* and the use of  
heterogenic

Schwann cells will be required. In the present study we addressed  
this

important issue and analysed the immunogenicity and survival of  
allogeneic

and xenogeneic Schwann cell suspension grafts in a prelesioned  
CNS fiber

tract, the transected postcommissural fornix of the adult Wistar rat.  
Cultured Schwann cells from Wistar rat or human peripheral nerve  
were

injected either immediately or after a delay into the transection site  
and

the spatio-temporal pattern of leukocyte infiltration and of major  
histocompatibility antigen expression was characterized and  
semi-quantified

with immunocytochemical methods. Our main findings are that (1)  
invasive

cerebral lesions induce the expression of MHC class I and II.  
antigens, but

only sparse infiltration of T-lymphocytes, (2) both allogeneic and  
xenogeneic discordant Schwann cell suspension grafts, from either  
neonatal

or adult peripheral nerve, survive without any overt signs of  
rejection

for up to 10 weeks after implantation; and (3) delayed implantation  
procedures have no effect on immune responses to allogeneic

Schwann cell

immune. These results demonstrate that there is no marked ongoing  
immune

reactions to heterogenic Schwann cell suspension grafts and that  
long-term survival of cross-species Schwann cell grafts can be

achieved in

the absence of any immunosuppressive treatment. Thus the  
conditions for

functional transplantation of Schwann cells across immunological  
barriers

seem to be favourable and will have implications for future  
cross-species

studies, and possibly also for clinical application.

L12 ANSWER 8 OF 28 MEDLINE

AN 97472951 MEDLINE

DN 97472951

TI The use of nonneuronal cells for gene delivery.

AU Snyder E Y; Senut M C

CS Department of Neurology, Harvard Medical School, Children's  
Hospital,

Boston, Massachusetts 02115, USA.

SO NEUROBIOLOGY OF DISEASE, (1997) 4 (2) 69-102. Ref:  
222

Journal code: CUN. ISSN: 0969-9961.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, ACADEMIC)

LA English

FS Priority Journals

EM 199801

EW 19980104

AB The implantation of genetically engineered nonneuronal cells can  
provide

an effective method for achieving localized delivery of discrete  
molecules

to the CNS or for providing substrates for regrowth of neural  
structures.

Most primary nonneuronal cells have the advantage of being easily  
obtainable from the prospective host for ex vivo

retrovirus-mediated

genetic manipulation (most will be mitotic in culture) and

reimplantation

as an autologous graft (circumventing the \*\*\*problem\*\*\* of  
immune

rejection). As primary cells, they are unlikely to be tumorigenic.  
The

most vexing \*\*\*problem\*\*\* for such systems remains the  
apparent loss

of transgene expression from viral promoters after prolonged  
periods of

engraftment. Much effort is currently being directed at optimizing  
sustained transgene expression by varying the promoters, by varying

the cell types to be engineered, or by regulating expression by  
enhancing

promoter function or substrate availability. While nonneuronal cells  
are

excellent vehicles for achieving passive delivery of substances to  
the

CNS, they lack the ability to incorporate into the host  
cytoarchitecture

in a functional manner (e.g., make synaptic contacts). For this  
reason,

not only may certain essential circuits not be re-formed, but the  
regulated release of certain substances through feedback loops may

be

missing. While apparently unimportant for some substances (e.g.,  
ACh), for

others (e.g., NGF), their unregulated, inappropriate, excessive, or

ectopic release may actually be inimical to the host. Furthermore,  
the  
loss of foreign gene expression (the bane of gene \*\*\*therapy\*\*\*  
) may

leave engineered nonneural \*\*\*cells\*\*\* incapacitated, whereas  
donor

tissue originating from brain may intrinsically produce various CNS  
factors allowing correction to proceed despite inactivation of the

introduced gene. In fact, CNS-derived tissue may provide  
as-yet-unrecognized endogenous neuralspecific substances which

are equally

as beneficial to the host as the gene in question. Thus, future  
developments in gene delivery to the brain for some conditions may

emphasize using \*\*\*neurons\*\*\* or neural progenitors for ex  
vivo

genetic manipulation (Fisher, 1997) and refining techniques for the  
direct

injection of therapeutic genes into \*\*\*neurons\*\*\* in vivo (see  
Snyder

and Fisher, 1996). For a wide variety of conditions, however, using  
nonneuronal cellular vehicles or even nonbiologic synthetic

vehicles may

be efficient, effective, and safe strategies for the passive delivery of  
therapeutic molecules to discrete regions of the CNS. In fact, this

approach may come closer than any other to immediate human  
applications.

L12 ANSWER 9 OF 28 MEDLINE

AN 97246615 MEDLINE

DN 97246615

TI Cellular and molecular \*\*\*neurosurgery\*\*\* : pathways from  
concept to

reality--part I: target disorders and concept approaches to gene  
therapy

of the central nervous system.

AU Zlokovic B V; Apuzzo M L

CS Department of Neurological Surgery, Childrens Hospital Los  
Angeles,

University of Southern California School of Medicine, USA.

SO NEUROSURGERY, (1997 Apr) 40 (4) 789-803; discussion  
803-4. Ref: 99

Journal code: NZL. ISSN: 0148-396X.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, ACADEMIC)

LA English

FS Priority Journals

EM 199709

EW 19970901

AB Recent advances in cellular and molecular biology and better  
understanding

of genetic and biochemical bases of different central nervous  
system (CNS)

disorders have made gene therapy of the CNS a realistic goal.  
Concept

approaches for gene therapy of CNS disorders are reviewed and

include the following: 1) gene replacement with a single normal allele to correct the inherited global \*\*\*neurodegenerative\*\*\* disorders, such as enzyme deficiencies; 2) brain repair to restore the function of a particular subset of cells that were lost because of a \*\*\*neurodegenerative\*\*\* process; 3) gene therapy of brain tumors; and 4) gene therapy of stroke.

Techniques of viral vector-mediated CNS transfer of a gene, transplantation of genetically modified \*\*\*cells\*\*\*, fetal embryonic implantation and/or implantation of genetically engineered neural progenitor cells, and production of a specific enzyme, \*\*\*neurotransmitter\*\*\*, and/or growth factor are discussed with respect to the therapeutic potential for global and localized CNS \*\*\*neurodegenerative\*\*\* disorders and stroke. Transfection of tumor cells with the drug susceptibility ("suicide") gene and/or gene and antisense strategies and a concept of adoptive immunotherapy of brain tumors are also discussed. Other approaches, such as transfer of drug-resistant genes and monoclonal antibody gene transfer, are briefly discussed. In addition to summarizing current principles of gene therapy for several groups of CNS disorders, the issues that remain to be resolved in clinical reality, such as delivery of the genetic material and regulation of the cellular expression of the transgene, and the negatives associated with the concepts of gene therapy, such as transient gene expression, toxicity of viral proteins, drawbacks of antisense therapy, and the \*\*\*problem\*\*\* of immune response to the transfected protein, have been also identified.

L12 ANSWER 10 OF 28 MEDLINE  
AN 97071954 MEDLINE  
DN 97071954  
TI Adenovirus for \*\*\*neurodegenerative\*\*\* diseases: in vivo strategies and ex vivo gene therapy using human neural progenitors  
AU Sabate O; Bartats M; Buc-Caron M H; Castel-Barthe M N; Finiels F; Horellou P; Revah F; Mallet J  
CS CNRS C 9923, Laboratoire de Genetique Moleculaire de la Neurotransmission  
Batiment et des Processus Degeratifs, Hopital de la Pitie, Salpêtrière  
Cervi, Paris, France.

SO CLINICAL NEUROSCIENCE, (1995-96) 3 (5) 317-21. Ref: 42  
Journal code: B9U. ISSN: 1065-6766.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LA English  
FS Priority Journals  
EM 199705  
EW 19970503  
AB The discovery of major \*\*\*neurodegenerative\*\*\* mechanisms has opened the way to the development of novel therapeutic approaches. Gene therapy now enables researchers to overcome certain \*\*\*problems\*\*\* inherent to pharmacotherapy and to the grafting of embryonic cells. The recombinant adenoviruses are promising for in vivo gene therapy involving \*\*\*neuroprotective\*\*\* (Ad-SOD), \*\*\*neurotrophic\*\*\* (Ad-NGF) as well as restorative (Ad-TH) strategies. In addition, human neural progenitors offer great potential as vehicles for ex vivo gene \*\*\*therapy\*\*\* to replace degenerated \*\*\*cells\*\*\* in advanced stages of \*\*\*neurodegenerative\*\*\* diseases. This paper describes the clinical values of the new generations of adenoviral vectors.

L12 ANSWER 11 OF 28 MEDLINE  
AN 96399809 MEDLINE  
DN 96399809  
TI [ \*\*\*Cell\*\*\* transplantation and gene \*\*\*therapy\*\*\* in Parkinson disease].  
Celltransplantation och genterapi vid Parkinsons sjukdom.  
AU Bjorklund A  
CS Wallenberg Neurocentrum, Institutionen for Fysiologi och Neurovetenskap, Lunds Universitet.  
Journal code: O4K. ISSN: 0029-1420.  
CY Sweden  
DT Journal; Article; (JOURNAL ARTICLE)  
LA Swedish  
EM 199701  
EW 19970104  
AB In 1995 the Anders Jahre Prize for medical research was shared by Professor Lars Olson, Stockholm (Nord Med 1996), and Professor Anders Bjorklund, Lund. Using newly developed methods, Anders Bjorklund has mapped important parts of the central nervous system and \*\*\*neurotransmitters\*\*\* in the brain. Bjorklund and co-workers

have therapeutically transplanted \*\*\*neurons\*\*\* to parts of the brain that, owing to disease or injury, are deficient in essential \*\*\*neurotransmitters\*\*\*. During recent years, the transplantation of fetal nerve cells has been introduced as a possible new therapeutic procedure in Parkinson's disease. Although promising results have been obtained in clinical trials both in Europe and North America, the technique needs further improvement to enhance cell survival, effectiveness and reproducibility. Moreover, an essential long-term goal is to eliminate dependence on a continuous supply of fetal tissue, which is both ethically and practically \*\*\*problematic\*\*\*. Current research is focused on ways to promote the survival and growth of grafted cells, and on the use of gene transfer procedures to generate alternative dopamine-producing of trophic factor-producing cells.

L12 ANSWER 12 OF 28 MEDLINE  
AN 96227618 MEDLINE  
DN 96227618  
TI [Insulin producing \*\*\*cells\*\*\* as \*\*\*therapy\*\*\* in diabetes mellitus].  
Insulinsenzemierende Zellen zur Therapie des Diabetes mellitus.  
AU Schnedl W J; Hohmeier H E; Newgard C B  
CS Medizinische Universitätsklinik, Karl Franzens Universität, Graz  
SO NATURWISSENSCHAFTEN, (1996 Jan) 83 (1) 1-5. Ref: 41  
Journal code: NSW. ISSN: 0028-1042.  
CY GERMANY; Germany, Federal Republic of  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LA German  
FS Priority Journals  
EM 199609  
AB Even with intensive insulin therapy it is impossible to reach physiological blood glucose levels in insulin-dependent diabetes mellitus. Because of the high costs and technical \*\*\*problems\*\*\* involved in islet \*\*\*cell\*\*\* transplantation broad applicability of this \*\*\*therapy\*\*\* seems uncertain. An alternative approach is the development of molecular-engineered insulin-producing clonal cell lines. The main interest is in rodent insulinoma cell lines and \*\*\*neuroendocrine\*\*\* A-T-20ins cells. This paper reviews the current knowledge about glucose-stimulated insulin secretion and the \*\*\*problems\*\*\* that have to be solved before these \*\*\*cells\*\*\* can be used for \*\*\*therapy\*\*\* in diabetes mellitus.

L12 ANSWER 13 OF 28 MEDLINE  
AN 96124619 MEDLINE

DN 96124619  
 TI Gaucher disease.  
 AU Onishi T  
 CS Jikei University School of Medicine, Department of Pediatrics.  
 SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1995 Dec) 53 (12)  
 2943-6. Ref: 12  
 Journal code: KIM. ISSN: 0047-1852.  
 CY Japan  
 DT Journal: Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA Japanese  
 EM 199605  
 AB Gaucher disease is an inherited metabolic disease characterized by deficient activity of lysosomal enzyme, known as a glucocerebrosidase.  
 Three clinical phenotype were documented depends on the onset of disease and \*\*\*neural\*\*\* involvement. Deficient activity of glucocerebrosidase results in progressive accumulation of glucocerebrosidase mainly in bone marrow derived macrophages. Diagnosis was made based on enzymatic activity in various tissue including WBC and fibroblasts. Molecular diagnosis was also possible. However, it is difficult to differentiate the three phenotypes. Although bone marrow transplantation and enzyme infusion therapy are both effective, the inherent \*\*\*problems\*\*\* limits their application. Gene therapy based on transfer of the \*\*\*therapeutic\*\*\* gene to hematopoietic stem \*\*\*cells\*\*\* were started in this year in USA.

L12 ANSWER 14 OF 28 MEDLINE  
 AN 96121848 MEDLINE  
 DN 96121848  
 TI Transplantation of microencapsulated hepatocytes for liver function replacement.  
 AU Dixit V; Gitnick G  
 CS UCLA School of Medicine, Department of Medicine  
 90024-7019, USA.  
 SO JOURNAL OF BIOMATERIALS SCIENCE, POLYMER EDITION, (1995) 7 (4) 343-57.  
 Journal code: AY7. ISSN: 0920-5063.  
 CY Netherlands  
 DT Journal: Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199603  
 AB Recent advances in cell biology and biotechnology have lead the way for a greater understanding of \*\*\*cell\*\*\* function and the potential \*\*\*therapeutic\*\*\* use of transplanted \*\*\*cells\*\*\* for

treating a wide array of illnesses. Treatment of disease by transplantation of normal healthy cells, for the replacement of specific biological deficiencies or as a form of auxiliary support for a failing organ, offers important therapeutic applications and also serves as a model for assessing cellular physiology. In the long-term, cell transplantation may also have potential in the development of artificial organ support systems for sustaining patients with severe and chronic diseases such as diabetes, liver failure, endocrine and exocrine disorders, \*\*\*neurological\*\*\* abnormalities, and congenital metabolic defects. Several groups have demonstrated the feasibility and efficacy of cell transplantation in providing specific function in various experimental animal models of human disease. However, without adequate immunosuppression, complications due to tissue rejection remain a significant \*\*\*problem\*\*\*. Microencapsulation of cells within a synthetic semipermeable membrane, prior to transplantation, has been proposed for circumventing immunological complications following transplantation. The microcapsule's semipermeable membrane allows permeant molecules to freely diffuse across while preventing the cells from escaping. This membrane also keeps unwanted substances, such as cells and antibodies, from entering the microcapsule. Thus, microencapsulation provides an innovative and unique technique for the transplantation of foreign tissue and cells without the need for immunosuppression.

L12 ANSWER 15 OF 28 MEDLINE  
 AN 96006511 MEDLINE  
 DN 96006511  
 TI A phase II trial of merbarone (NSC 336628) as salvage \*\*\*therapy\*\*\* for squamous \*\*\*cell\*\*\* carcinoma of the cervix. A Gynecologic Oncology Group Study.  
 AU Look K Y; Blessing J A; Williams L; Morris M  
 CS Department of Obstetrics and Gynecology, Indiana University School of Medicine, Indianapolis, USA.  
 NC CA 27469 (NCI)  
 CA 37517 (NCI)  
 SO AMERICAN JOURNAL OF CLINICAL ONCOLOGY, (1995 Oct) 18 (5) 441-3.  
 Journal code: 3EZ. ISSN: 0777-3732.  
 CY United States

DT (CLINICAL TRIAL, PHASE II)  
 Journal: Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals; Cancer Journals  
 EM 199601  
 AB Twenty-seven patients with previously irradiated unresectable recurrent squamous carcinoma of the cervix who had failed one prior cytotoxic regimen received 1,000 mg/m2 per day of merbarone given by continuous i.v. infusion for 5 days every 4 weeks through a central line. One patient was never treated, and four were inevaluable for response, leaving 26 patients evaluable for toxicity and 22 evaluable for response. The major adverse effect was myelosuppression with 6/26 (23%) experiencing Gynecologic Oncology Group (GOG) grade 3 or 4 leukopenia. There were two episodes (3.8%) of GOG grade 3 SGOT elevation. There were two patients (9.0%) who developed mental status changes classified as grade 3 \*\*\*neurotoxicity\*\*\*. This \*\*\*neurotoxicity\*\*\* may have been secondary to iatrogenic hyponatremia caused by the large volumes of 5% glucose infusion required at the original infusate concentration. After the concentration of the merbarone infusate was increased to 4 mg/ml, no further \*\*\*problems\*\*\* with hyponatremic \*\*\*neurotoxicity\*\*\* were encountered. The overall response rate was 2/22 (9.0%) (95% confidence interval 1.1-29.2%). In this pretreated population with recurrent squamous cervical carcinoma, merbarone exhibited only minimal activity.

L12 ANSWER 16 OF 28 MEDLINE  
 AN 94281278 MEDLINE  
 DN 94281278  
 TI Recent advances in diagnosis and treatment of small cell and non-small cell lung cancer.  
 AU Sorensen J B; Hansen H H  
 CS Department of Oncology, National University Hospital/Rigshospitalet, Copenhagen, Denmark.  
 SO CURRENT OPINION IN ONCOLOGY, (1994 Mar) 6 (2) 162-70. Ref: 63  
 Journal code: A1V. ISSN: 1040-8746.  
 CY United States  
 DT Journal: Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA English  
FS Priority Journals  
EM 199409  
AB Despite much effort and many published reports, progress in diagnosing and treating lung cancer has been slow. The use of monoclonal antibodies for detection of metastasis and \*\*\*neuroendocrine\*\*\* markers for subclassification of non-small cell lung cancer into different prognostic groups may be useful in future staging and treatment.  
Dose-intensive chemotherapy in small cell lung cancer is still experimental, which is also the case for prophylactic cranial irradiation. Adjuvant chemotherapy for completely resected patients with non-small cell lung cancer may be associated with a marginal survival benefit, which also seems to hold true for patients with advanced disease when compared with untreated control subjects solely receiving supportive care. The modest survival benefit is achieved at the cost of increased toxicity. Neoadjuvant treatment remains a controversial issue, one of the major \*\*\*problems\*\*\* being the lack of an effective standard systemic \*\*\*therapy\*\*\* in non-small \*\*\*cell\*\*\* lung cancer.

L12 ANSWER 17 OF 28 MEDLINE  
AN 94116614 MEDLINE  
DN 94116614  
TI A model three-dimensional culture system for mammalian dopaminergic precursor cells: application for functional intracerebral transplantation.  
AU Spector D H; Boss B D; Strecker R E  
CS Department of Psychiatry and Behavioral Science, SUNY at Stony Brook  
11794.  
SO EXPERIMENTAL NEUROLOGY, (1993 Dec) 124 (2) 253-64.  
Journal code: EQF. ISSN: 0014-4886.

CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199404  
AB Grafts of fetal neural tissue, rich in dopamine (DA) \*\*\*neurons\*\*\*, have previously been shown to improve the symptoms of parkinsonism, both in humans and in animal models. In order to circumvent some of the \*\*\*problems\*\*\* associated with \*\*\*cell\*\*\* transplant

\*\*\*therapy\*\*\*, such as the limited availability of transplant tissue, we have established a reaggregate (three-dimensional) tissue culture system that can be used to proliferate normal mammalian \*\*\*neural\*\*\* precursors.  
We demonstrate the in vitro growth of DA- \*\*\*neural\*\*\* precursors derived from embryonic porcine ventral mesencephalon, Carnegie stages 15-18. Cultures of DA- \*\*\*neural\*\*\* precursors were maintained in F12 medium supplemented with Chang C Supplement for 5 days and switched to serum-free N2 medium for an additional 10 days. Cultures labeled with tritiated thymidine on Days 5-7 in vitro revealed that 43.5% of the DA \*\*\*neurons\*\*\* had incorporated the label, indicative of cell division.  
Histological examination of the cultured cells demonstrated rosette-like structures, similar to developing \*\*\*neuroepithelium\*\*\* in vivo.  
\*\*\*Neural\*\*\* maturation in vitro was stimulated by dibutyryl cyclic AMP (dbcAMP). Exposure to 5 mM dbcAMP for 7 days stimulated tyrosine hydroxylase (TH), \*\*\*neuron\*\*\*-specific enolase, and 200-kDa \*\*\*neurofilament\*\*\* accumulation three- to sixfold above control levels.  
After 15 days in vitro, cultured cells reversed amphetamine-induced rotation when grafted into the striata of hemiparkinsonian rats. Successful transplants of cultured \*\*\*neurons\*\*\* were dependent upon a minimum density of DA \*\*\*neurons\*\*\* within the graft (greater than 100 DA \*\*\*neurons\*\*\* /mm<sup>3</sup> of graft volume). Data suggest that the percentage of TH \*\*\*neurons\*\*\* can be increased about threefold by culturing the aggregates in tyrosine-free medium, which selects for TH-positive cells. The ability to cultivate mammalian \*\*\*neural\*\*\* precursor cells in vitro may eventually make graft therapy a more practical approach to treatment of \*\*\*neurological\*\*\* diseases.  
L12 ANSWER 18 OF 28 MEDLINE  
AN 94057845 MEDLINE  
DN 94057845  
TI Neural stem cells for CNS transplantation.  
AU Baegje E E  
CS CytoTherapeutics, Inc., Providence, Rhode Island 02906.  
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1993 Sep 24) 695 285-91.  
Ref: 27  
Journal code: SNM. ISSN: 0077-8923.  
CY United States

DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LA English  
FS Priority Journals; Cancer Journals  
EM 199402  
AB \*\*\*Neurodegenerative\*\*\* disorders such as Parkinson's, Alzheimer's, and Huntington's disease are becoming ever more prominent in our society.  
A direct approach towards therapeutic treatment of these diseases is through replacement therapy where normal tissue is transplanted back to the nervous system. Recently, significant progress has been achieved with transplants in Parkinson's disease, but the process is heavily dependent on an unstable and \*\*\*problematic\*\*\* source of fetal tissue.  
Neural stem cells may become the tissue/ \*\*\*cell\*\*\* source necessary for developing the \*\*\*therapeutic\*\*\* potential of neural transplantation.  
Stem \*\*\*cells\*\*\* are self-renewing, multipotent and could provide a well-characterized and clean source of transplantable material. A number of new in vitro approaches have led to the development of continuously propagated stem cells that are potential candidates for nervous system transplantation. These include oncogene-induced immortalization and growth-factor stimulation of naturally occurring central and peripheral nervous system stem cells. The nature of these cells and their suitability for transplantation into the CNS will be evaluated.  
L12 ANSWER 19 OF 28 MEDLINE  
AN 92146986 MEDLINE  
DN 92146986  
TI Integrative assessment of the developmental pharmacology and developmental toxicology, with special reference to the brain.  
AU Fujii T  
CS Department of Pharmacology, Teikyo University School of Medicine, Tokyo, Japan.  
SO NIPPON YAKURIGAKU ZASSHI. FOLIA PHARMACOLOGICA JAPONICA, (1991 Dec) 98 (6) 419-34. Ref: 92  
Journal code: F2X. ISSN: 0015-5691.  
CY Japan  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)



- LA Japanese  
FS Priority Journals  
EM 199205  
AB Increasing numbers of \*\*\*neurotoxins\*\*\* or \*\*\*therapeutic\*\*\* agents that have specific target \*\*\*cells\*\*\* or receptors can be used to assess the developmental correlation between the structure and function of various organs including the brain. Patients with chronic diseases are now able to maintain their social activities but still must be medicated for a long period of their life. This might increase the potential hazard of prenatal drug exposure in the progeny. Functional teratology is quite a new concept in \*\*\*neuroscience\*\*\*. Recent observations of our laboratory and those of others suggest that the sensitive period for functional teratology might encompass the whole stage of fetal life in animals and humans. The shortage of precise information on the developmental integration of the structure and function of the \*\*\*neurons\*\*\* with different properties is a \*\*\*problem\*\*\* to be solved for the further progress of developmental pharmacology and toxicology. Single exposures to drugs at a different stage during the gestational period of rats or mice might provide more useful information on the relationship between the lesioned area and related functional disorders manifested postnatally. This paper reviews recent advances in development. \*\*\*neuropharmacology\*\*\* and functional \*\*\*neuroteratology\*\*\* including beneficial points of the short-term exposures to drugs.
- L12 ANSWER 20 OF 28 MEDLINE  
AN 92117468 MEDLINE  
DN 92117468  
TI [Rare tumor of the postero-superior mediastinum. Therapeutic approach. Apropos of a case. Review of the literature].  
Tumeur rare du mediastin postero-superieur. Attitude therapeutique. A propos d'un cas. Revue de la litterature.  
AU Zimmermann J M; De Graeve B; Cador L; Colonna M A; Coblenz J F; Lemesle L  
CS Polyclinique Clairval, Marseille.  
SO ANNALES DE CHIRURGIE, (1991) 45 (8) 695-8. Ref: 36  
Journal code: 50E. ISSN: 0003-3944.  
CY France  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW LITERATURE)  
LA French  
EM 199204
- AB The authors report an exceptional case of giant cell tumour of the third thoracic vertebra revealed by its mediastinal development. Despite intimate involvement of the large mediastinal vessels, a double surgical approach, starting with sternotomy to ensure vascular control then anterolateral thoracotomy, allowed curative resection of this tumor. Treatment was completed by a second \*\*\*neurosurgical\*\*\* operation followed by 5,000 rads of radiotherapy. Based on a review of the literature, the authors discuss the pathogenesis and consider the various \*\*\*therapeutic\*\*\* \*\*\*problems\*\*\* raised by giant \*\*\*cell\*\*\* tumours of the vertebrae (situated above the sacrum).
- L12 ANSWER 21 OF 28 MEDLINE  
AN 92097077 MEDLINE  
DN 92097077  
TI Double screening of suramin derivatives on human colon cancer cells and on neural \*\*\*cells\*\*\* provides new \*\*\*therapeutic\*\*\* agents with reduced toxicity.  
AU Baghdigian S; Nickel P; Fantini J  
CS INSERM U270, Faculty of Medicine, Marseille, France.  
SO CANCER LETTERS, (1991 Dec 1) 60 (3) 213-9.  
Journal code: CMX. ISSN: 0304-3835.  
CY Netherlands  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; Cancer Journals  
EM 199204  
AB Suramin is a polyanionic compound currently used under evaluation for antineoplastic activity. One of the main \*\*\*problems\*\*\* encountered during clinical trials was an adverse \*\*\*neurotoxic\*\*\* effect, probably due to a direct cytotoxic effect on neural cells. Suramin is also known to trigger differentiation of human colon cancer cells, yet a chronic treatment induces a lysosomal storage disorder. The aim of this study was to evaluate suramin analogs for their effect: (i) on the lysosomal system of the human colon cancer cell clone HT29-D4; and (ii) on C6 glioma cell growth and morphology. One of the derivatives NF036, induced terminal differentiation of HT29-D4 cells without any impairment of the lysosomal system. Furthermore, in contrast to suramin, NF036 did not alter C6 cell growth and morphology. We conclude that there is a relationship between the ability of a suramin derivative to induce a lysosomal storage disorder in human colon cancer cells and its
- \*\*\*neurotoxic\*\*\* effect. A double screening of suramin analogs on HT29-D4 and C6 cells allowed us to identify a new candidate antineoplastic drug: NF036.
- L12 ANSWER 22 OF 28 MEDLINE  
AN 91056694 MEDLINE  
DN 91056694  
TI A case of long-term survival of a patient with complicated diffuse metastatic leptomeningeal carcinomatosis secondary to lung adenocarcinoma.  
AU Watanabe A; Mizobe M; Ogawa Y; Takei N; Nomoto H; Urata C; Mano K; Hohjo S; Imamura T  
CS Second Department of Internal Medicine, Teikyo University, School of Medicine, Tokyo, Japan.  
SO NIHON KYOBU SHIKKAN GAKKAI ZASSHI. JAPANESE JOURNAL OF THORACIC DISEASES, (1990 Aug) 28 (8) 1130-5.  
Journal code: KQD. ISSN: 0301-1542.  
CY Japan  
DT Journal; Article; (JOURNAL ARTICLE)  
LA Japanese  
EM 199103  
AB A case of long-term survival of a female patient with complicated diffuse metastatic leptomeningeal carcinomatosis (DMLC) secondary to lung cancer is reported. A 36-year-old woman, hospitalized with a chief complaint of headache and unproductive cough, was diagnosed as having primary lung adenocarcinoma (T4N1M1 oss) and was given systemic chemotherapy. Although progressive deterioration of her headache continued, repeated \*\*\*neurological\*\*\* examination, cerebrospinal fluid (CSF) examination, and cranial CT scans failed to show evidence of metastasis to the central nervous system, and the only finding suggesting CNS involvement was an elevated CEA level in CSF. Later in the course of her treatment, the patient suddenly lost her vision and subsequently consciousness due to acute increased intracranial pressure, and emergency ventricular drainage was performed for \*\*\*therapeutic\*\*\* and diagnostic purposes. Malignant \*\*\*cells\*\*\* were found in CSF obtained from a ventricular drainage and she was treated successfully by systemic and intrathecal chemotherapeutic agents. She was discharged after a ventriculoperitoneal shunt operation.

for hydrocephalus; a double-dome reservoir was used for continuous intrathecal administration of the anticancer drugs, and a shunt filter was located in the tube to prevent the dissemination of cancer cells. In addition to methotrexate and cytosine arabinoside, ACNU and interleukin-2 were administered intrathecally without serious adverse effects, but no apparent therapeutic effects were noted either. She survived over 2 years after DMCLC was first diagnosed. At autopsy DMCLC secondary to lung adenocarcinoma was confirmed, but no evidence of leukoencephalopathy due to aggressive intrathecal chemotherapy was found. Current therapy for patients with DMCLC and its clinical \*\*\*problems\*\*\* are discussed in relation to our experience in this case.

L12 ANSWER 23 OF 28 MEDLINE  
AN 88309709 MEDLINE  
DN 88309709  
TI History of \*\*\*neuroblastoma\*\*\* involving bone marrow: the \*\*\*problem\*\*\* of detecting residual tumour after initiation of chemotherapy.  
AU Reid M M; Hamilton P J  
CS Department of Haematology, Royal Victoria Infirmary, Newcastle upon Tyne.  
SO BRITISH JOURNAL OF HAEMATOLOGY, (1988 Aug) 69 (4) 487-90.  
Journal code: AXC. ISSN: 0007-1048.

CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; Cancer Journals  
EM 198812  
AB One hundred and eighty bone marrow trephine biopsies obtained during 68 staging procedures before and during treatment of 20 children with Stage IV \*\*\*neuroblastoma\*\*\* were reviewed. A primitive cell infiltrate with prominent fibrous stromal reaction and increased reticulin characterized the marrow at presentation. Once treatment had begun, primitive cells became difficult to find but fibrosis and a marked increase in reticulin persisted in most cases. Distortion in marrow architecture and the continuation of abnormal stromal reactions may reflect failure to eradicate tumour despite absence of detectable primitive \*\*\*cells\*\*\*.  
If current \*\*\*therapeutic\*\*\* options are to be assessed properly, uniformly accepted criteria to define continuance of marrow infiltration

in children with \*\*\*neuroblastoma\*\*\* are needed. A scheme for classifying marrow histological appearances is presented which may prove to be of more value than a simple distinction between 'involved' and 'uninvolved'.

L12 ANSWER 24 OF 28 MEDLINE  
AN 88289199 MEDLINE  
DN 88289199  
TI Intraventricular gamma-globulin for the management of enterovirus encephalitis.  
AU Dwyer J M; Ertlindsson K  
CS Department of Clinical Immunology, Yale University School of Medicine, New Haven, CT.  
SO PEDIATRIC INFECTIOUS DISEASE JOURNAL, (1988 May) 7 (5 Suppl) S30-3. Ref: 11

Journal code: OXJ. ISSN: 0891-3668.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW OF REPORTED CASES)  
LA English  
FS Priority Journals  
EM 198811

AB Although bacterial infections predominate in patients with hypogammaglobulinemia, patients who do not produce normal amounts of immunoglobulin also have an increased incidence of viral infections. This is particularly true of infections with enteroviruses. Echovirus encephalitis has been a major \*\*\*problem\*\*\* for patients with hypogammaglobulinemia. \*\*\*Neurologic\*\*\* damage, frequently resulting in death, has been common in such patients. Because there is an obligatory extracellular phase in the \*\*\*cell\*\*\* to \*\*\*cell\*\*\* spread of enteroviruses, \*\*\*therapy\*\*\* with immunoglobulin has been attempted. In certain patients intravenous and intrathecal gammaglobulin has temporarily halted progression of the disease, but no patients have been cured by this approach. In this report we detail treatment of three children with X-linked hypogammaglobulinemia who had encephalitis caused by echovirus infections. Despite doses of intravenous immunoglobulin that maintained the patients' IgG levels within the normal range, their condition deteriorated in all cases. Treatment with intraventricular immunoglobulin was then tried. In all three cases cerebrospinal fluid protein levels and cell counts returned to normal after this treatment and the echoviruses can no longer be isolated from the cerebrospinal fluid.

Follow-up time has ranged from 18 months to 4 years. Ommaya reservoirs were placed into the lateral ventricle of each patient and concentrated (6%) immunoglobulin (Sandoglobulin) was injected into the reservoir on a daily basis. On Days 1 through 7 of the regimen patients were given 120, 300, 450, 510, 540 and 600 mg of IgG, respectively. Patients then received 300 mg daily for periods ranging from 1 week to 1 month. Cultures of cerebrospinal fluid removed from the reservoir were repeatedly analyzed to determine the need for further treatment. Clinically the patients improved markedly (ABSTRACT TRUNCATED AT 250 WORDS)

L12 ANSWER 25 OF 28 MEDLINE  
AN 88282438 MEDLINE  
DN 88282438  
TI Augmentation of cell number and LAK activity in peripheral blood mononuclear cells activated with anti-CD3 and interleukin-2.  
Preliminary results in children with acute lymphocytic leukemia and \*\*\*neuroblastoma\*\*\*.  
AU Anderson P M; Bach F H; Ochoa A C  
CS Immunobiology Research Center, University of Minnesota, Minneapolis 55455.  
NC T32CA09445 (NCI) A117687 (NIAID) A118326 (NIAID) +

SO CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1988) 27 (1) 82-8.  
Journal code: CN3. ISSN: 0340-7004.  
CY GERMANY, WEST. Germany. Federal Republic of  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; Cancer Journals  
EM 198811  
AB A wide variety of human cancers currently have no effective treatment and are potential targets for lymphokine-activated killer (LAK) cellular immunotherapy. Relapsed acute lymphocytic leukemia (ALL) and \*\*\*neuroblastoma\*\*\* are two of the major therapeutic challenges in pediatric oncology today. However, one \*\*\*problem\*\*\* which makes LAK immunotherapy in children particularly difficult is obtaining the large numbers of \*\*\*cells\*\*\* required. Present adult \*\*\*therapeutic\*\*\* LAK protocols have utilized short-term (5 day) cultures of (IL2)-activated cells which are initially obtained from

#### leukopheresis.

Since routine use of this procedure in small children is not practical, we have investigated a different approach to obtain increased cell numbers by activation of peripheral blood mononuclear cells with OKT3, a mitogenic anti-CD3 monoclonal antibody, and IL2. Cell growth and LAK activity in OKT3 + IL2-activated cultures were compared to cultures activated with IL2 alone in 2 children with relapsed ALL and 2 children with stage IV \*\*\*neuroblastoma\*\*\*. OKT3 + IL2-activated cultures had marked increases in cell number: after 14 days the OKT3 + IL2-activated cultures yielded an approximately 500-fold increase in cell number compared to a 7-fold increase for cultures activated with IL2 alone. In vitro 51Cr release assays were used to estimate LAK activity of the cultures at 7 and 14 days. When tested against HL60, a natural killer (NK)-resistant tumor cell line, not only were total cytolytic units greatly increased in OKT3 + IL2-stimulated cultures by lytic activity on a per cell basis (lytic units/1 x 10(6) cells) had also markedly increased on day 14 of culture. Phenotypic analysis demonstrated that 80% to 90% of cells in OKT3 + IL2-stimulated cultures were CD3 + T cells. Variable low percentages of CD16 + NK cells were seen in these cultures. In summary, OKT3 + IL2 activation resulted in a large increase in cell yield and the development of high level LAK activity using peripheral blood mononuclear cells from children with cancer. This approach may facilitate the utilization of increased cell numbers in future adoptive immunotherapy protocols, especially in pediatric patients.

L12 ANSWER 26 OF 28 MEDLINE

AN 87089581 MEDLINE

DN 87089581

TI \*\*\*Neuroendocrine\*\*\* aspects of pineal tumors.

AU Fetti M R, Stein B M

SO NEUROLOGIC CLINICS, (1986 Nov) 4 (4) 877-905.

Journal code: NEU. ISSN: 0733-8619.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198704

AB The evaluation and treatment of pineal region tumors has

changed

dramatically in the past decade. New imaging techniques result in

#### earlier

diagnosis. Surgical techniques now permit removal of benign tumors (about one third of cases). Pathologic diagnosis is obtained for the remainder, and postoperative \*\*\*therapy\*\*\* can be planned rationally. Germ \*\*\*cell\*\*\* tumors pose a particularly difficult \*\*\*problem\*\*\* for the pathologist because they often contain mixed germ cell elements. Biologic markers, beta HCG and AFP, aid diagnosis and can be monitored in serum and CSF to assess response to treatment. Only boys develop precocious puberty with pineal tumors. What appears to be puberty is actually pseudoprecocious puberty, due to ectopic production of HCG by their neoplasms (choriocarcinomas or germinomas with syncytiotrophoblastic giant cells). HCG can stimulate tests to produce testosterone, but FSH is necessary (together with LH or HCG) to stimulate ovaries to produce estrogen. Diabetes insipidus, with pineal tumors is usually due to spread to the hypothalamus by ventricular seeding, but we report a case of aqueductal stenosis with diabetes insipidus resulting from a massively dilated third ventricle. Rarely, hydrocephalus may trigger true precocious puberty, a syndrome easily differentiated from pseudoprecocious puberty by endocrinologic tests. There are no biologic markers to diagnose pineal parenchymal tumors. Elevation of melatonin in plasma or CSF and tumor biosynthetic activity has been reported in isolated cases, but the range of melatonin values in normals is very wide, and melatonin levels do not correlate with specific pathologic tumor types. Both parenchymal and nonparenchymal tumors may increase melatonin nonspecifically by interfering with regulatory mechanisms of the normal pineal gland.

L12 ANSWER 27 OF 28 MEDLINE

AN 84304245 MEDLINE

DN 84304245

TI Long-term survival and toxicity in small cell lung cancer.

Southwest

Oncology Group study.

AU Livingston R B, Stephens R L, Bonnet J D, Grozea P N, Lehane

DE

NC CA-20319 (NCI)

CA-12644 (NCI)

CA-28862 (NCI)

+

SO AMERICAN JOURNAL OF MEDICINE, (1984 Sep) 77 (3) 415-7.

Journal code: 3JU. ISSN: 0002-9343.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals

EM 198412

AB In the first study of combined chemotherapy and radiation

\*\*\*therapy\*\*\*

for small \*\*\*cell\*\*\* lung cancer by the Southwest Oncology

Group, 17

patients survived more than five years after treatment was initiated

(4.6

percent). Late relapse, or a second primary malignancy three to six

years

after diagnosis, accounted for death in five of these patients. Late

recurrences involved the chest, bone, and liver; none occurred in

the

central nervous system. Disease-free survival continues in 10

patients (6

percent of those with limited disease and 1 percent of those with

extensive-stage diseases) at a minimal follow-up in excess of six

years.

One definite case of chronic treatment-related toxicity occurred:

congestive cardiomyopathy after 450 mg/m2 of doxorubicin,

successfully

managed with digitalis and diuretics. One severe

\*\*\*neurologic\*\*\*

\*\*\*problem\*\*\* (orthostatic hypotension with preterminal

dementia) and

two less severe \*\*\*neurologic\*\*\* complications (occasional

falling

episodes without documented cause and cerebrovascular accident)

may be

treatment-related. Progressive pulmonary disability, post-herpetic

pain

syndromes, organic brain syndrome, and hematologic abnormalities

have not

been observed to date. Nitrosourea administration and/or

co-administration

of a nitrosourea or methotrexate during the induction phase of

treatment

with radiotherapy to the brain may account for the higher incidence

of

complications observed by others in long-term survivors.

L12 ANSWER 28 OF 28 MEDLINE

AN 82084383 MEDLINE

DN 82084383

TI [Contamination of a glioma by the herpes virus]

Contamination d'un gliome par le virus herpetique.

AU Ochsner F

SO SCHWEIZER ARCHIV FUR NEUROLOGIE,

NEUROCHIRURGIE UND PSYCHIATRIE, (1981)

129 (1) 19-30.  
 Journal code: UDS. ISSN: 0036-7273.  
 CY Switzerland  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA French  
 FS Priority Journals  
 EM 198204  
 AB The clinical and \*\*\*neuropathologic\*\*\* descriptions of a glioma in a 65 years old patient, who died 9 days after its subtotal resection, are documented. The post-mortem study of the brain revealed an herpetic encephalitis with its classical topographical distribution. There were numerous eosinophilic inclusion bodies which ultrastructurally were characteristic of herpes simplex virus. The author discusses, with reference to the literature, the exo and endogenous sources of infection, the means of dissemination, the \*\*\*problem\*\*\* of latency and reactivation of the virus. He proposes the hypothesis that the infection of the glioma cells is this case was most likely related the immature immunity of the \*\*\*cells\*\*\*, corticoid \*\*\*therapy\*\*\* and surgical resection acting as inducers. The almost complete absence of an inflammatory reaction evokes an opportunistic viral infection in an immunodeficient patient. Inspite of the description by many authors of different particles which have been interpreted as of viral origin in some brain tumours, the hypothesis of an oncogenic action of the herpetic virus is not retained in this particular case, considered as exceptional, of the glioma described herein. The precocious search for HSV antibodies by immunofluorescence and a temporal lobe biopsy in order to establish an early diagnosis are necessities so as to administer as rapidly as possible the specific therapy, adenine-arabinside.

=> d his

(FILE 'HOME' ENTERED AT 09:21:39 ON 20 SEP 1999)  
 FILE 'CAPLUS' ENTERED AT 09:21:46 ON 20 SEP 1999  
 L1 1331380 S REVIEW/DT  
 L2 7686 S (CELL7(3A)(THERAP7)/AB,BI  
 L3 1401 S L1 AND L2  
 L4 4796 S (CELL7(3A)(THERAP7)/AB,BI  
 L5 918 S L4 AND L1  
 L6 41 S L3 AND ADMINIST7/AB,BI  
 L7 1 S L6 AND NEURO7/AB,BI

L8 277 S L4 AND NEURO7/AB,BI  
 L9 485 S L2 AND NEURO7/AB,BI  
 L10 66 S L9 AND L1  
 FILE 'MEDLINE' ENTERED AT 09:30:39 ON 20 SEP 1999  
 L11 539 S L9  
 L12 28 S L11 AND (UNPREDICT7 OR PROBLEM7)/AB,BI  
 =>  
 ---Logging off of STN---  
 =>  
 Executing the logoff script...  
 => LOG Y  

COST IN U.S. DOLLARS	ENTRY	SINCE FILE	TOTAL
FULL ESTIMATED COST	8.66	SESSION	95.35

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)  
 SINCE FILE TOTAL  
 CA SUBSCRIBER PRICE 0.00 -16.60  
 STN INTERNATIONAL LOGOFF AT 09:38:30 ON 20 SEP 1999